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- USPC 604/509, 507, 22; 606/194
See application file for complete search history.

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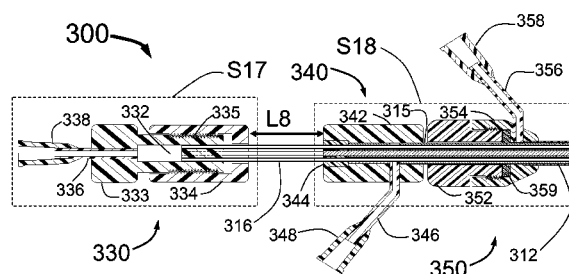
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- (57) **ABSTRACT**

A catheter-based/intravascular fluid injection system with application to renal denervation includes a multiplicity of needles which expand open around a central axis to engage the wall of a blood vessel, or the wall of the left atrium, allowing the injection of a cytotoxic and/or neurotoxic solution for ablating conducting tissue, or nerve fibers around the ostium of the pulmonary vein, or circumferentially in or just beyond the outer layer of the renal artery. The expandable delivery system includes expandable components that facilitate positioning of a multiplicity of injection needles against the inside wall of a blood vessel from where they can be advanced. The system also includes means to limit and/or adjust the depth of penetration of the ablative fluid into the tissue of the wall of the targeted blood vessel.

49 Claims, 22 Drawing Sheets



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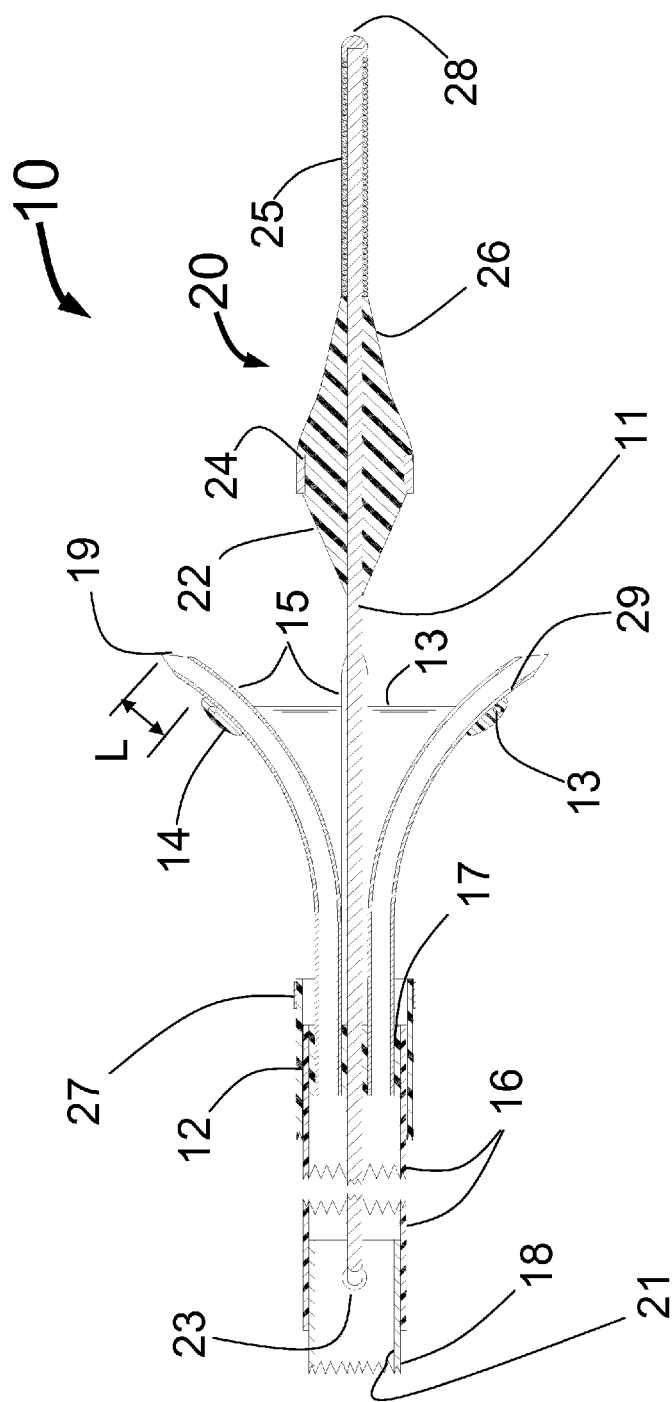
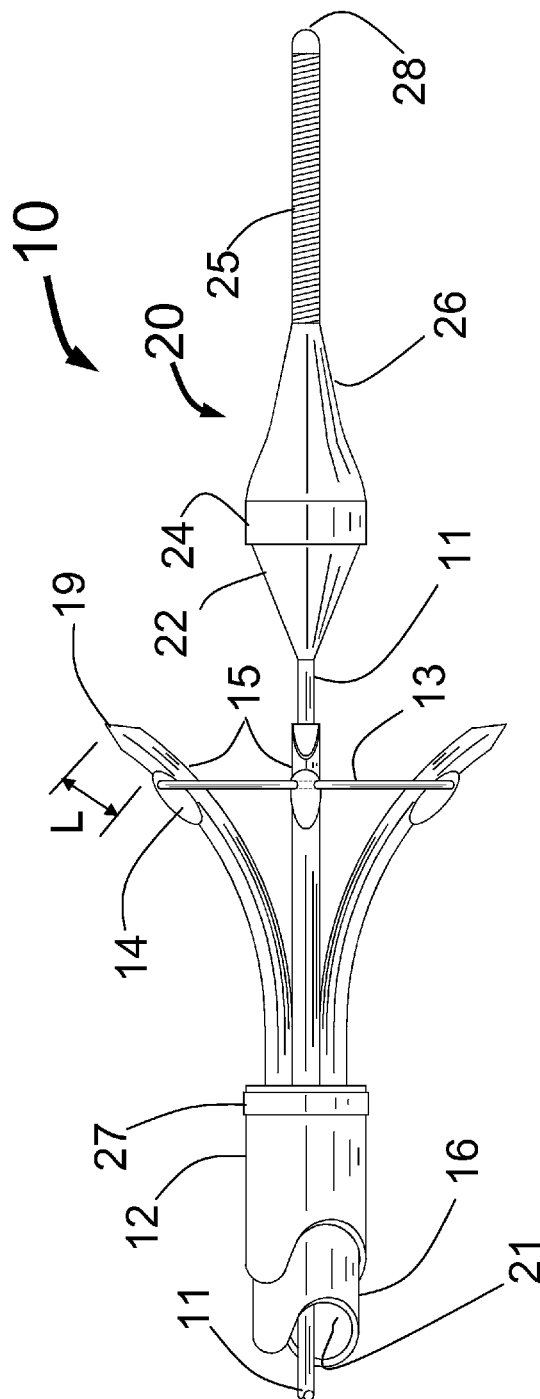
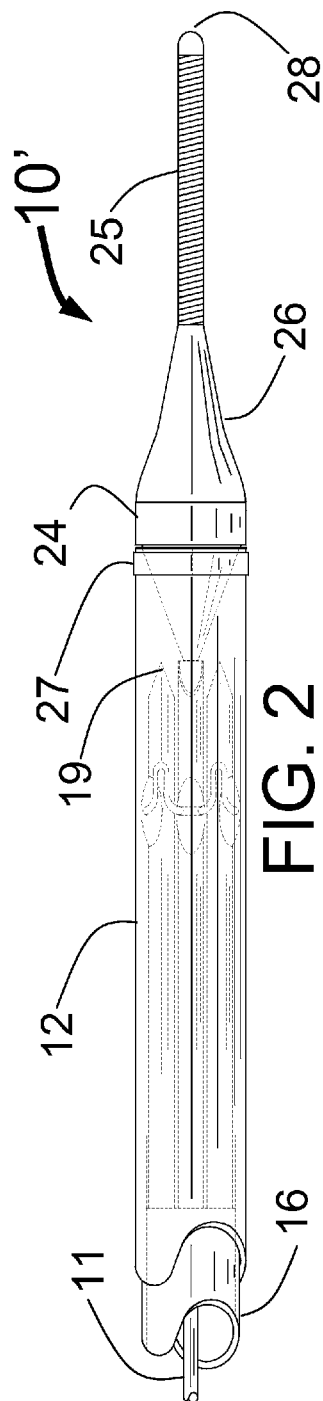
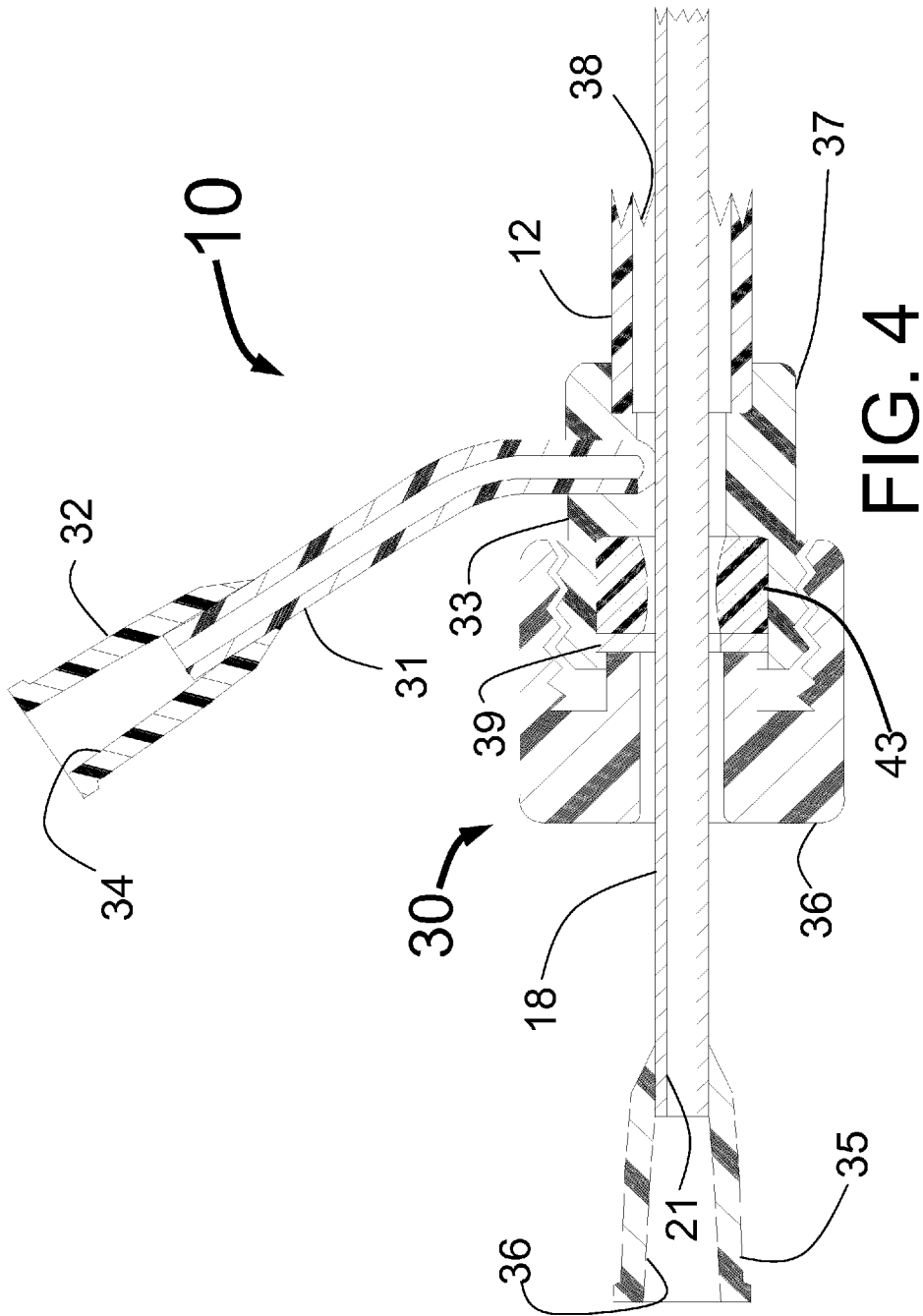


FIG. 1





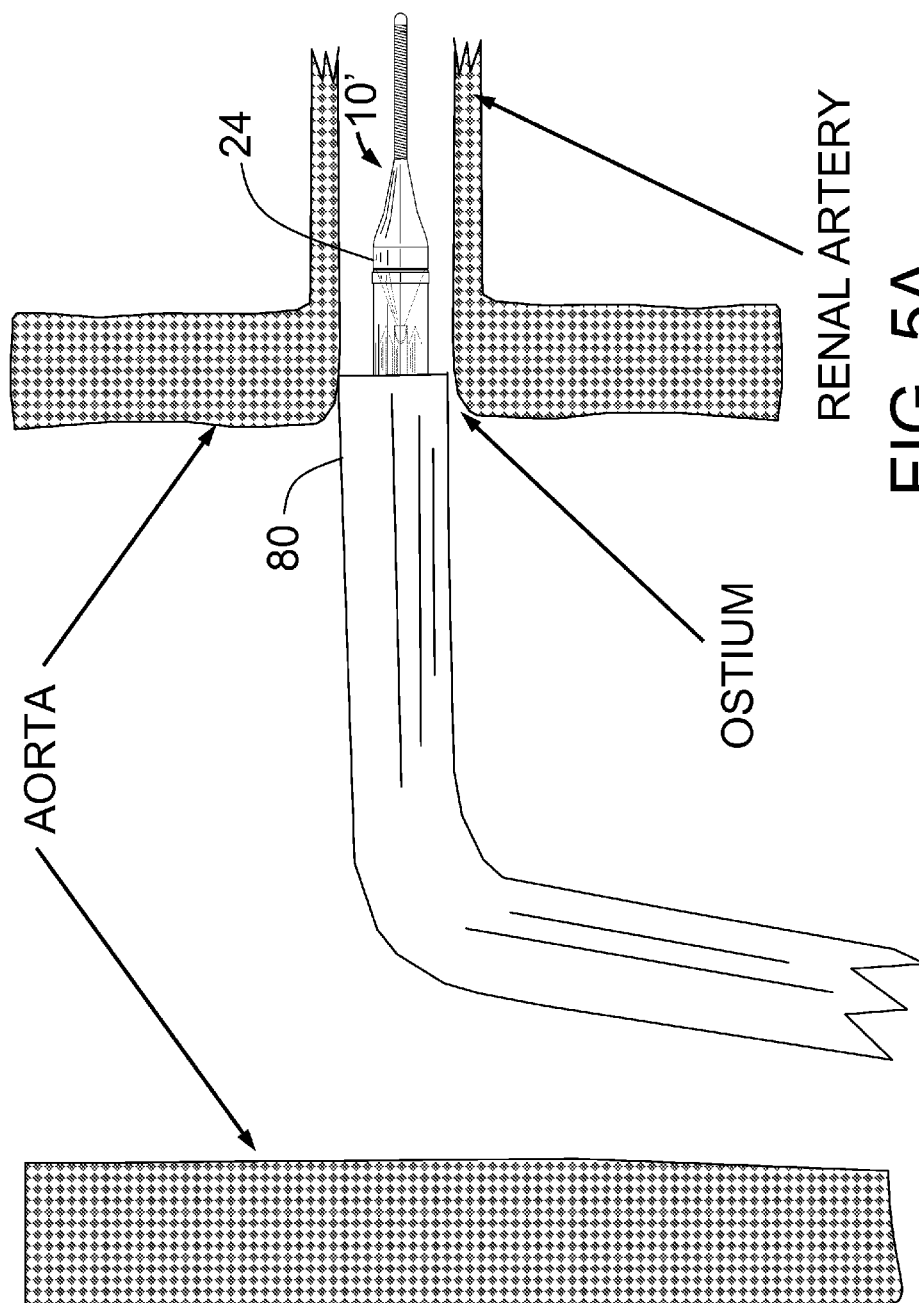
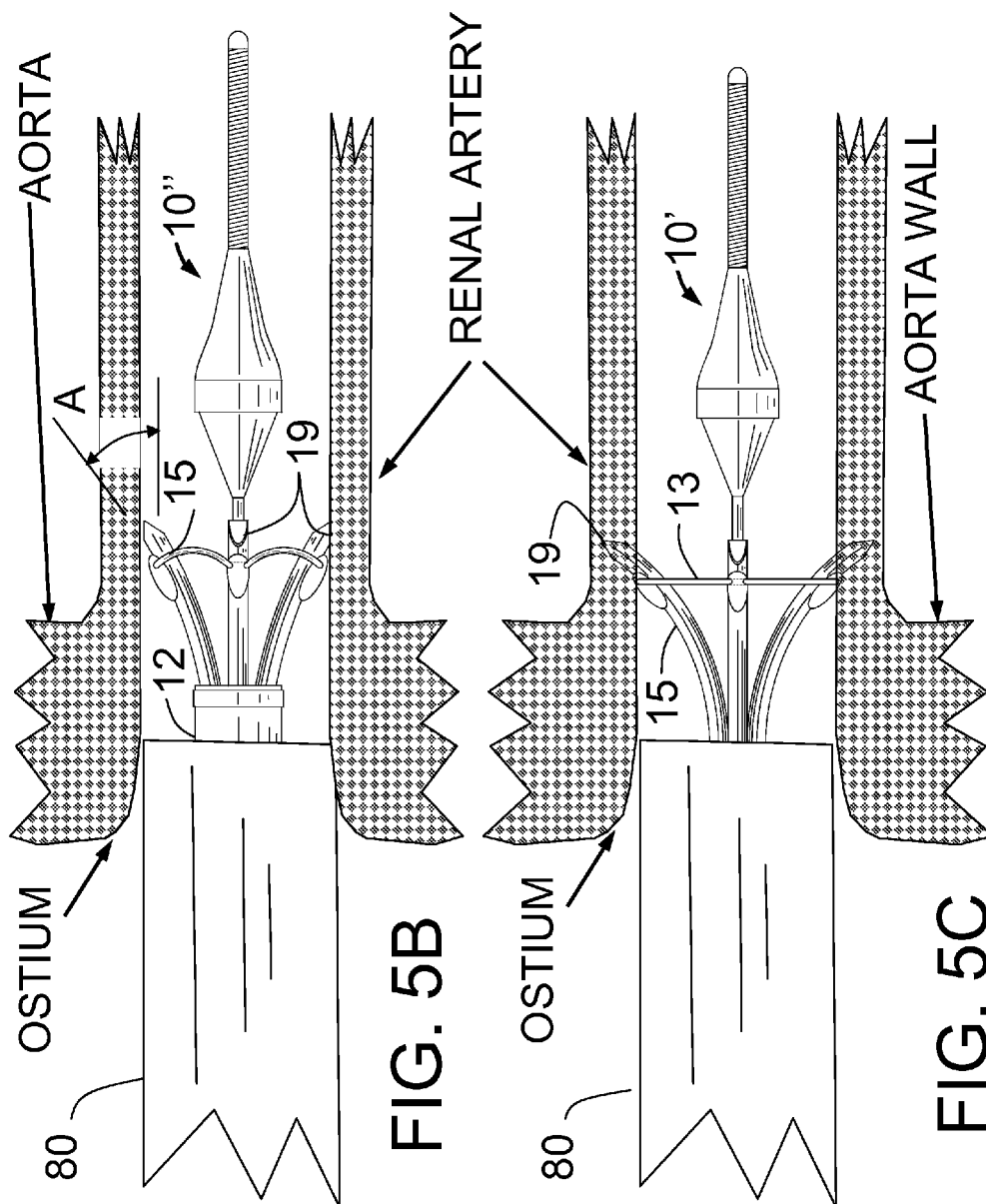
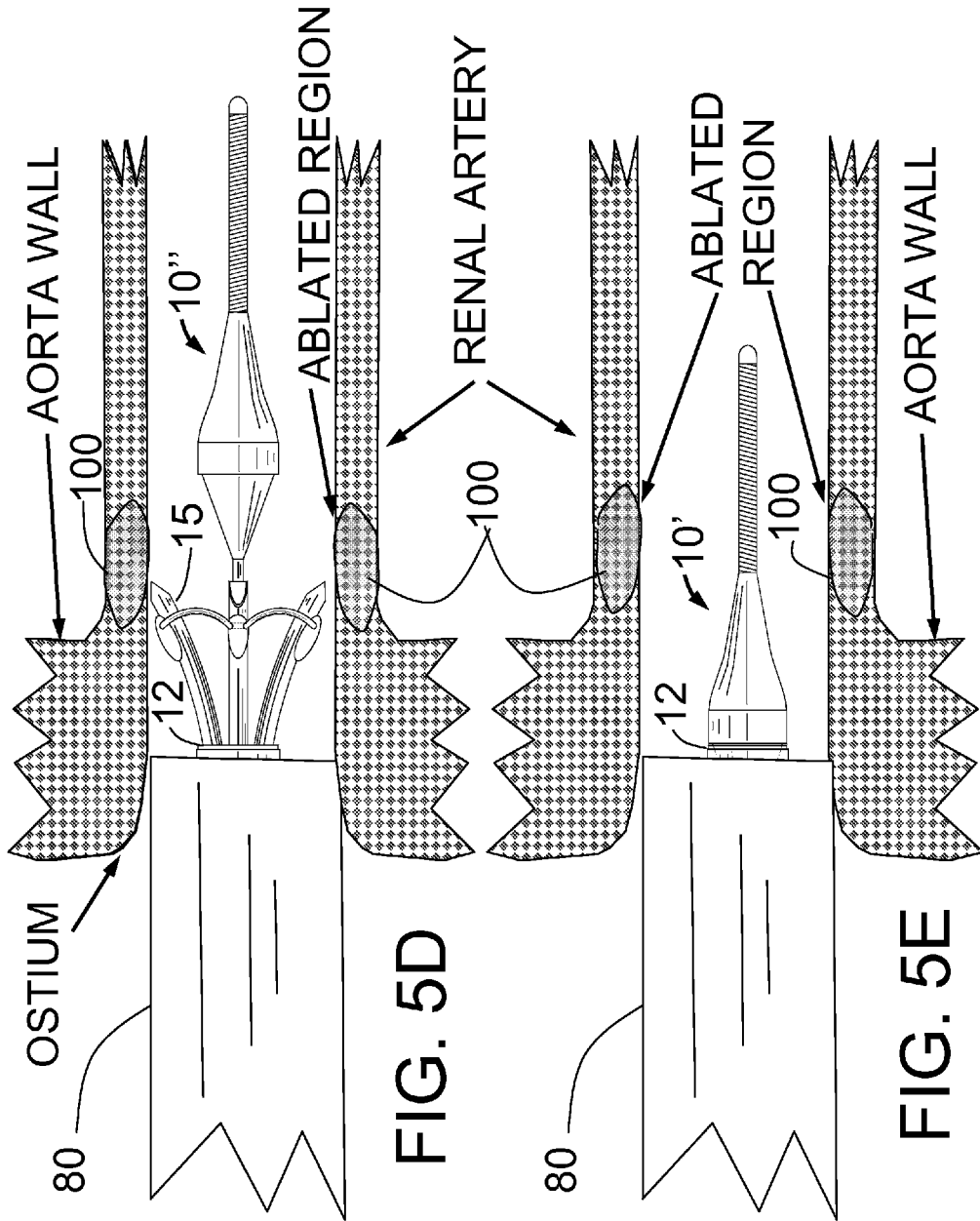


FIG. 5A





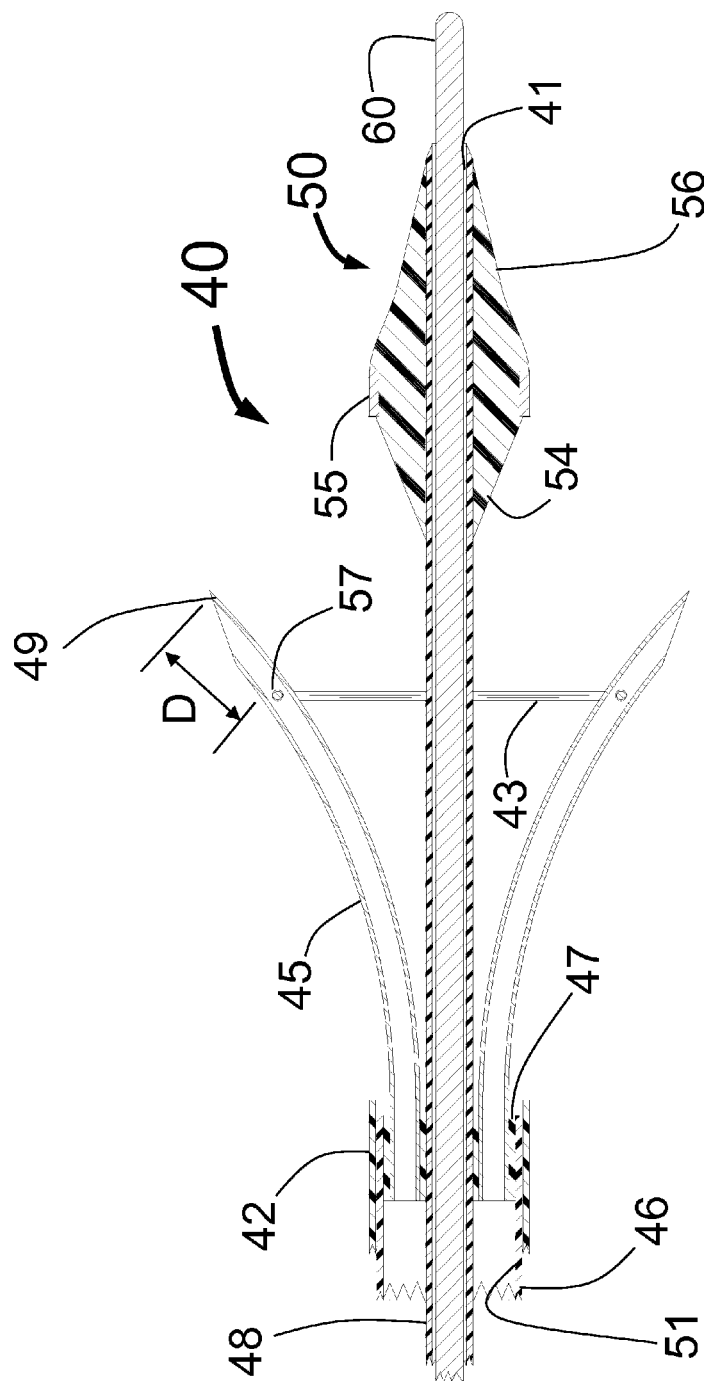
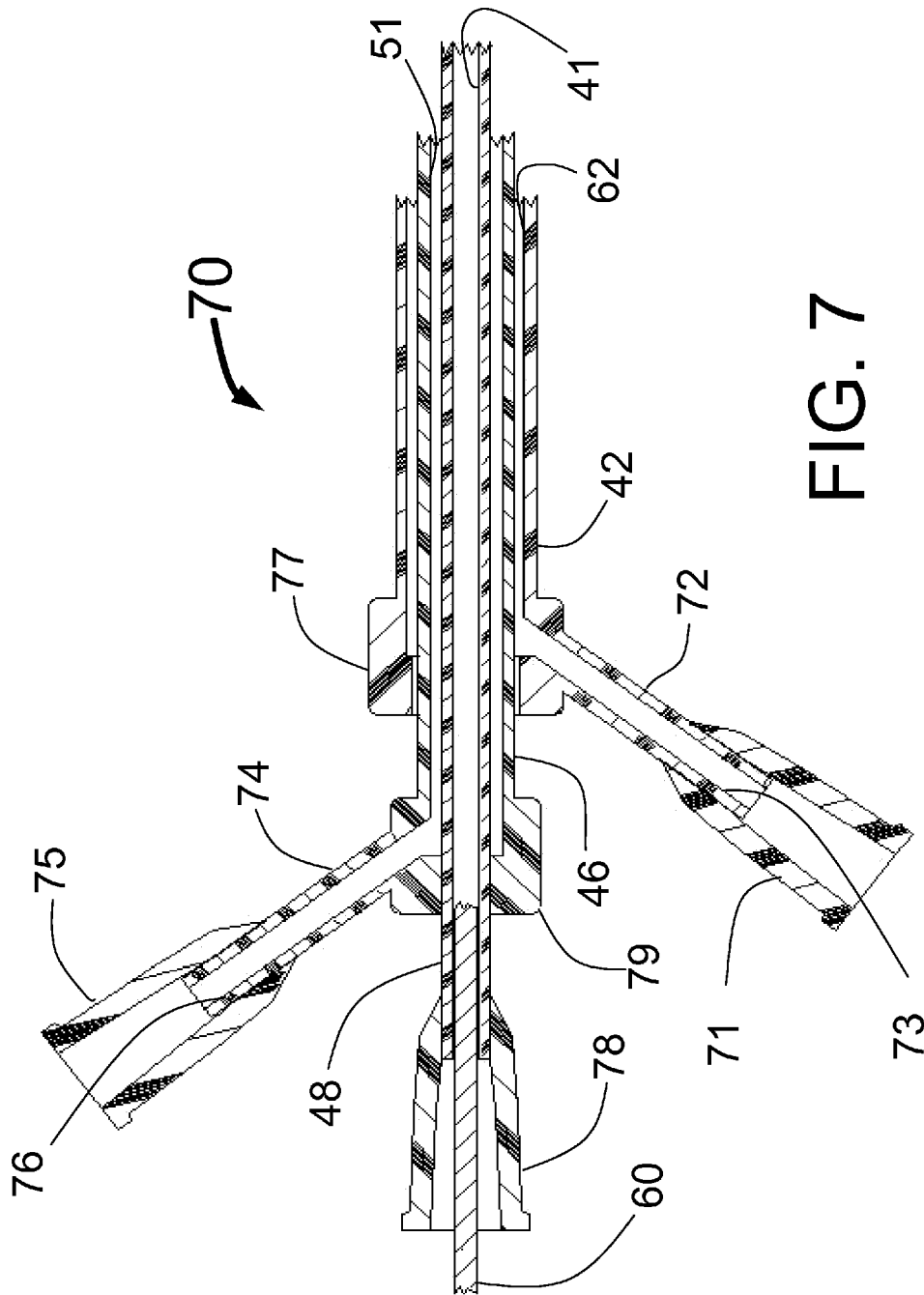
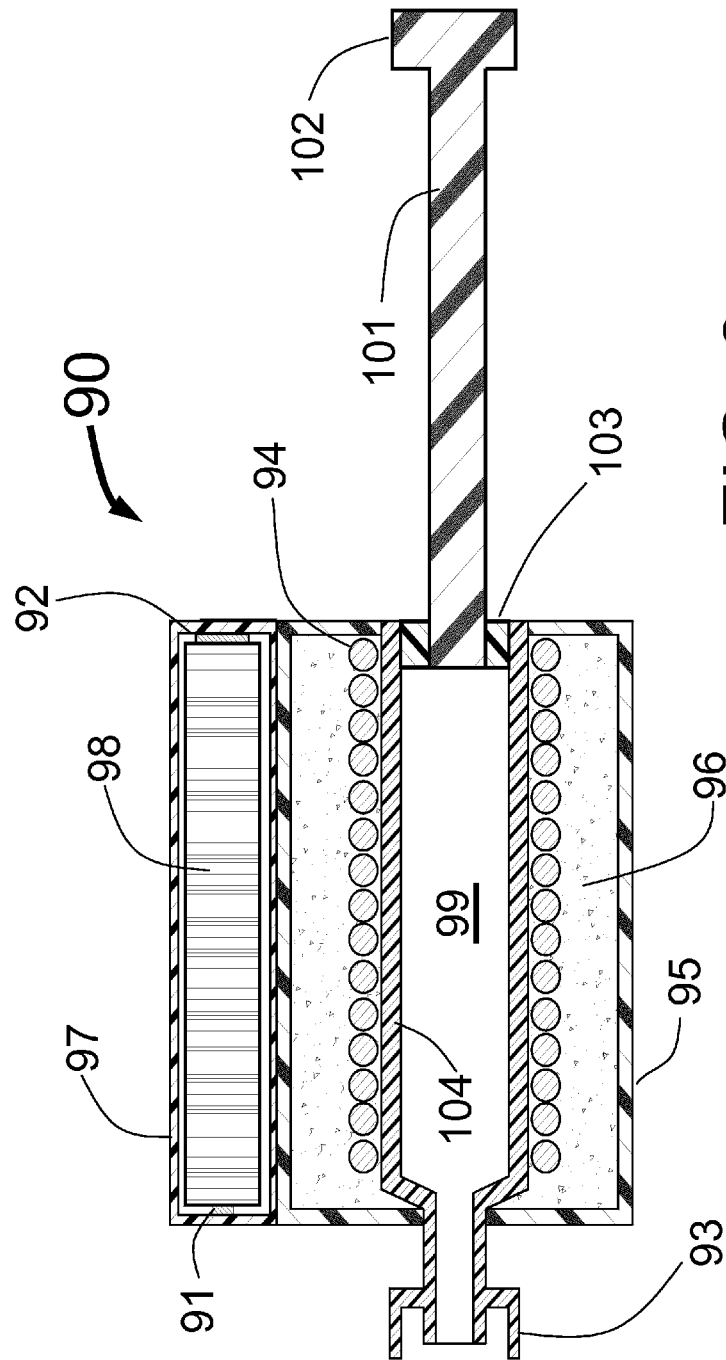


FIG. 6




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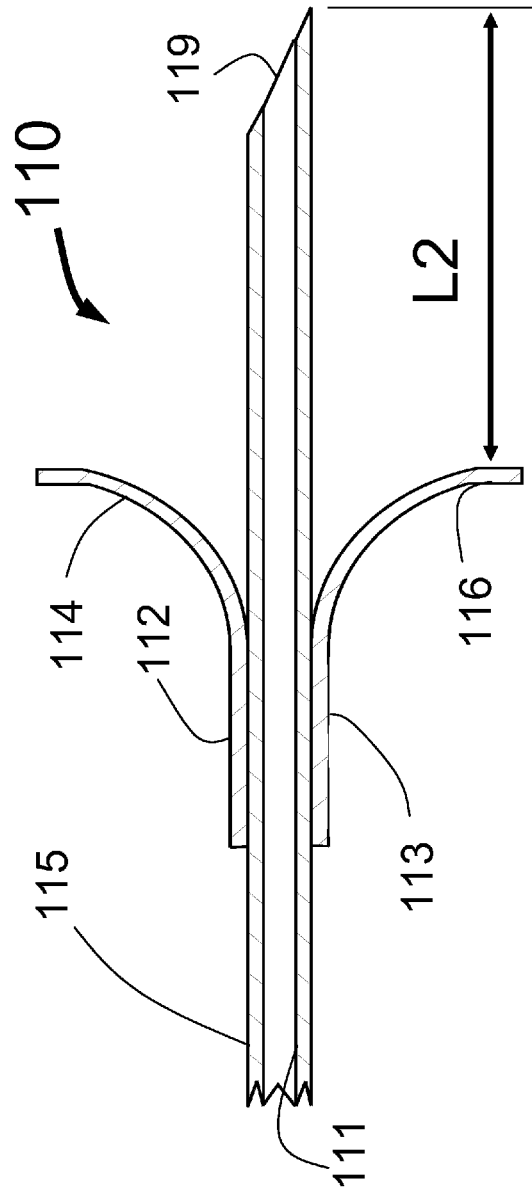


FIG. 9

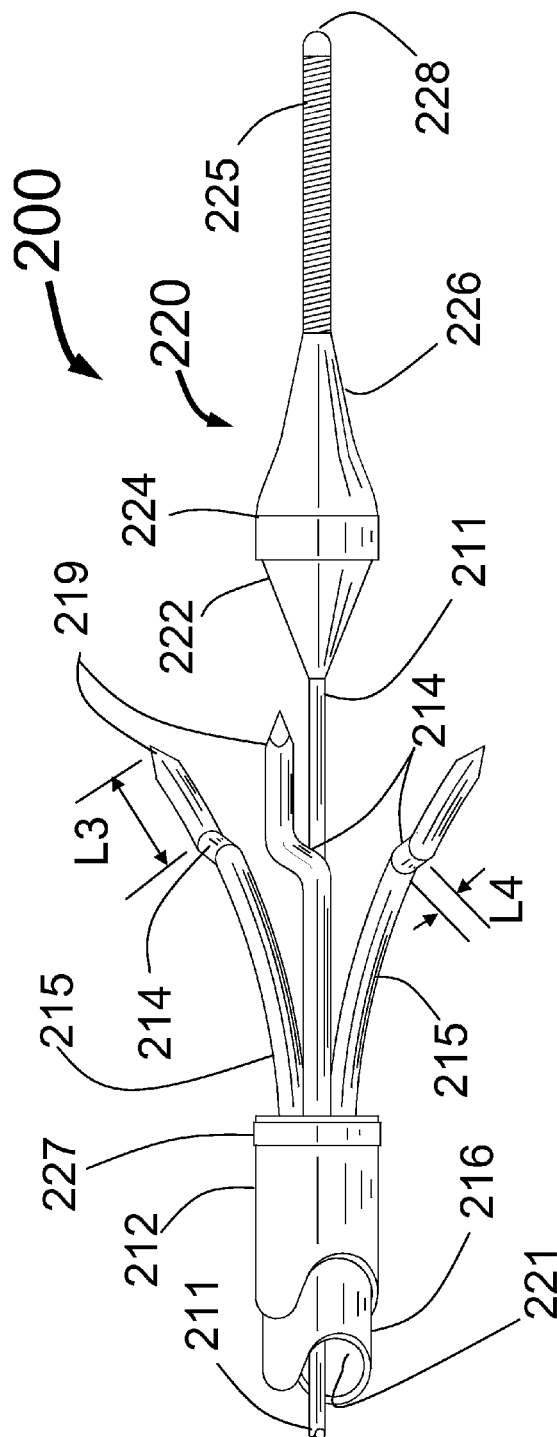


FIG. 10

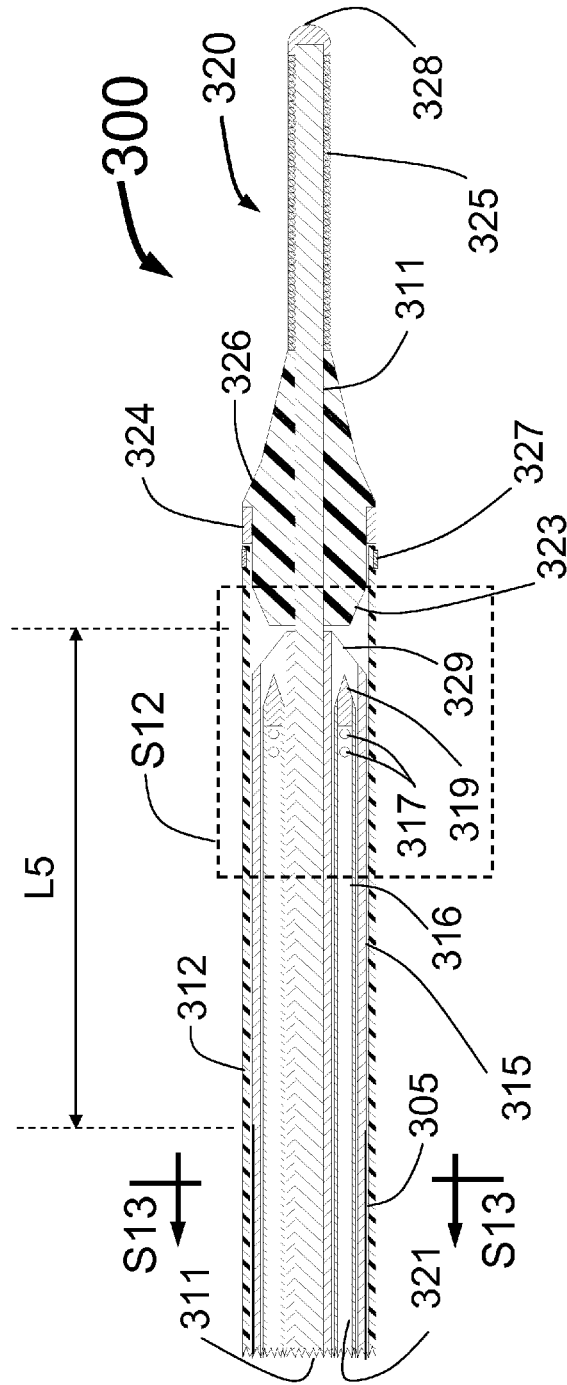


FIG. 11

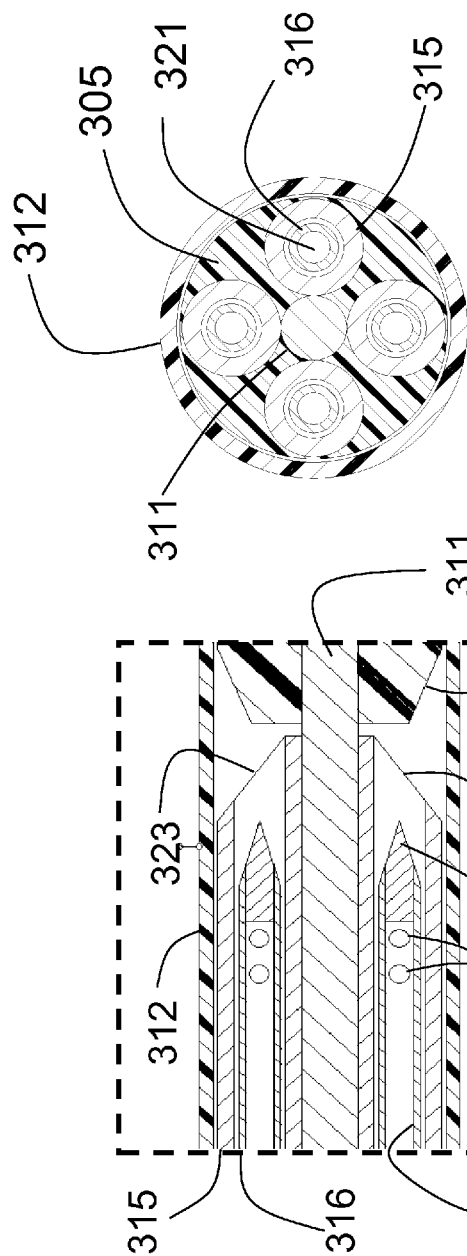


FIG. 13

FIG. 12

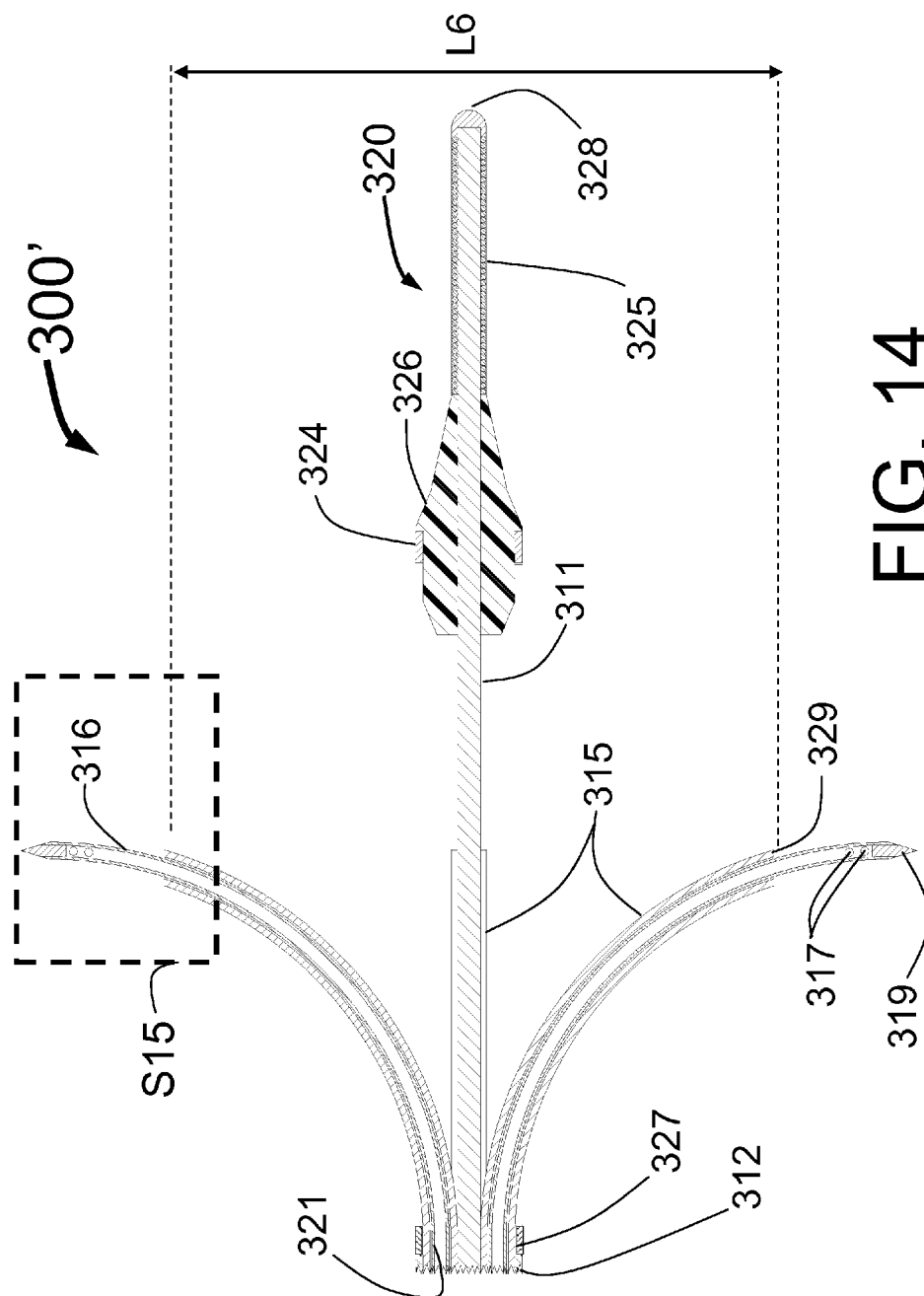
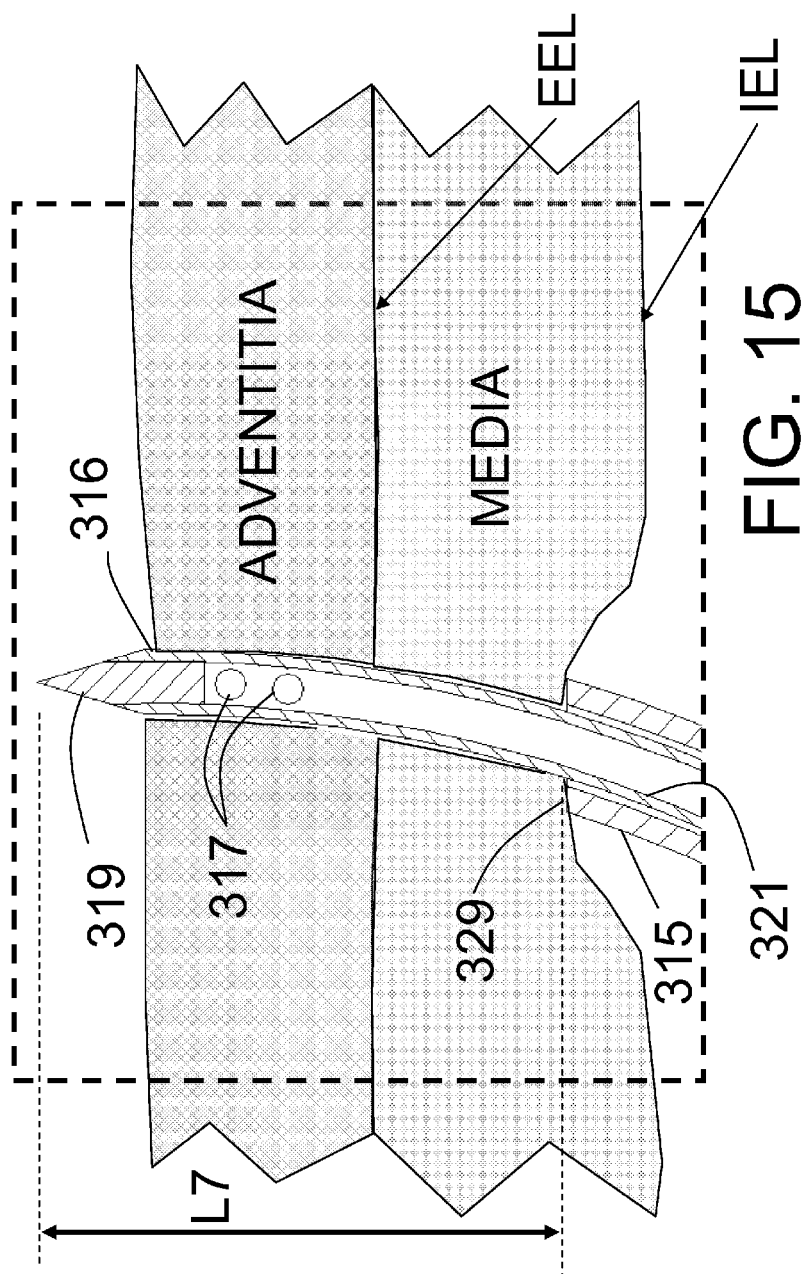


FIG. 14



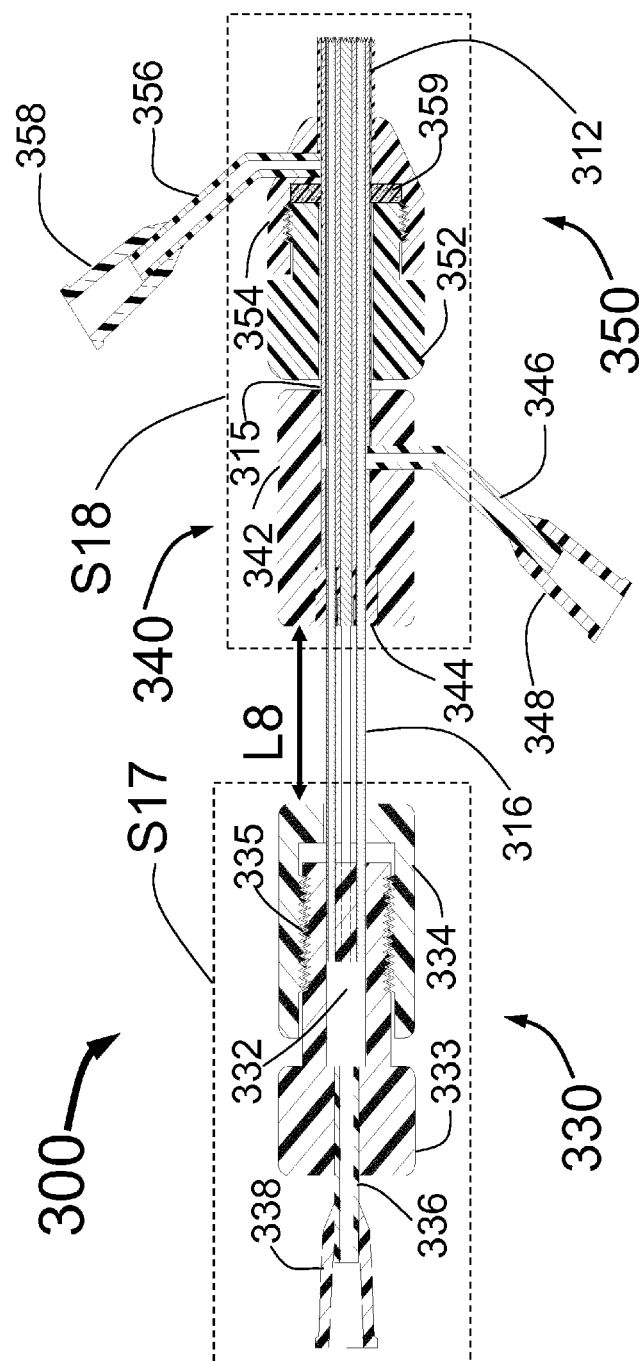


FIG. 16

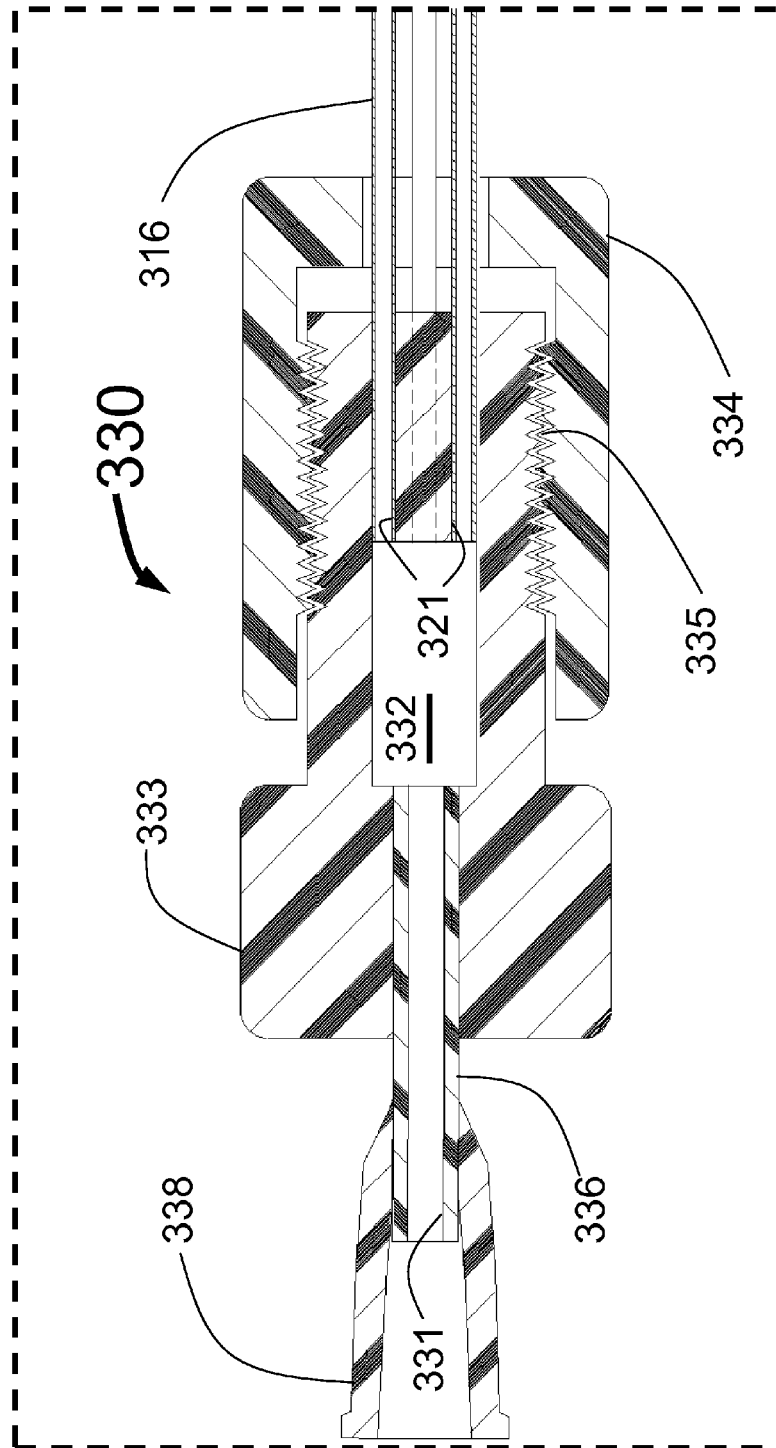


FIG. 17

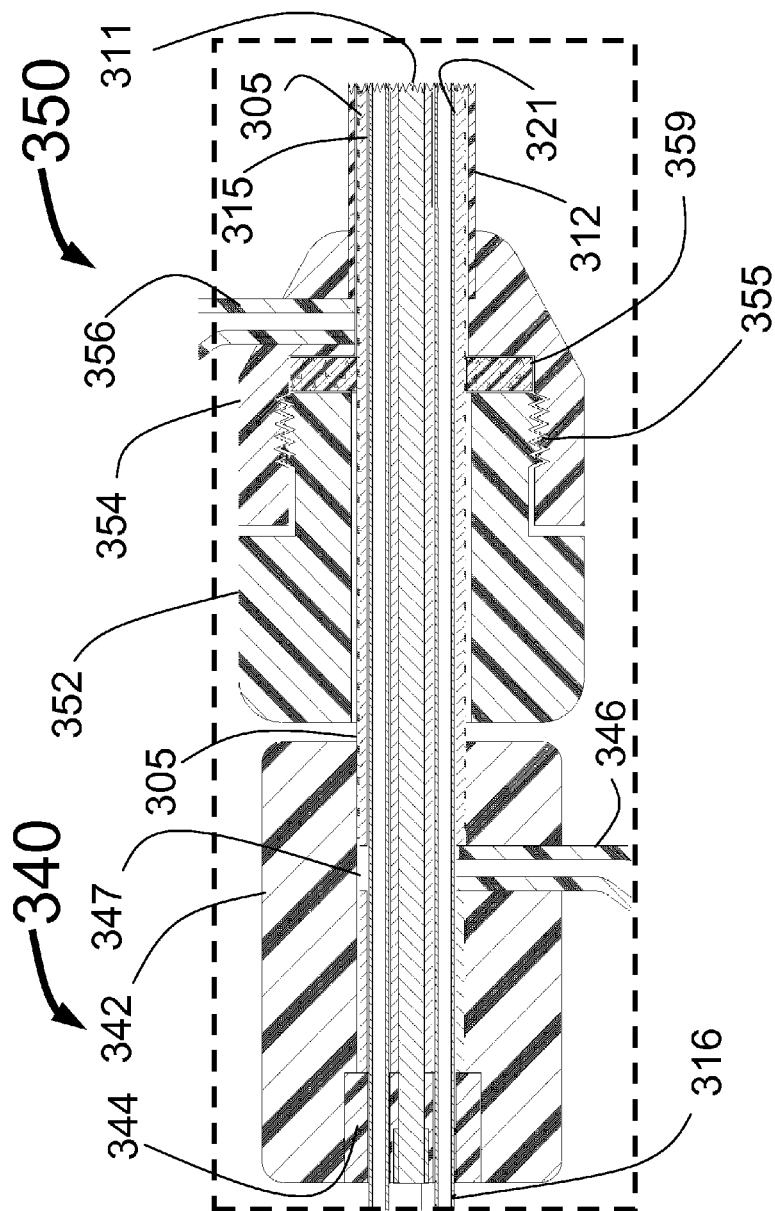


FIG. 18

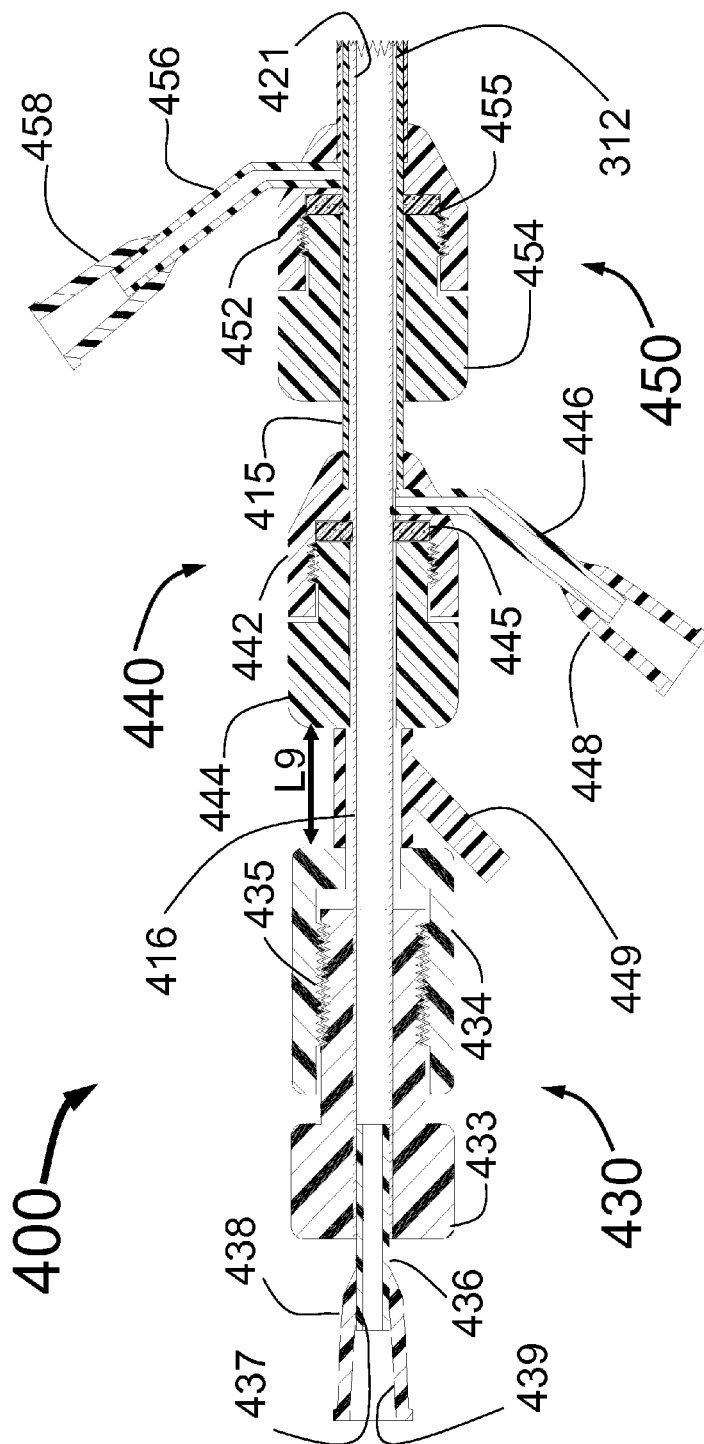


FIG. 19

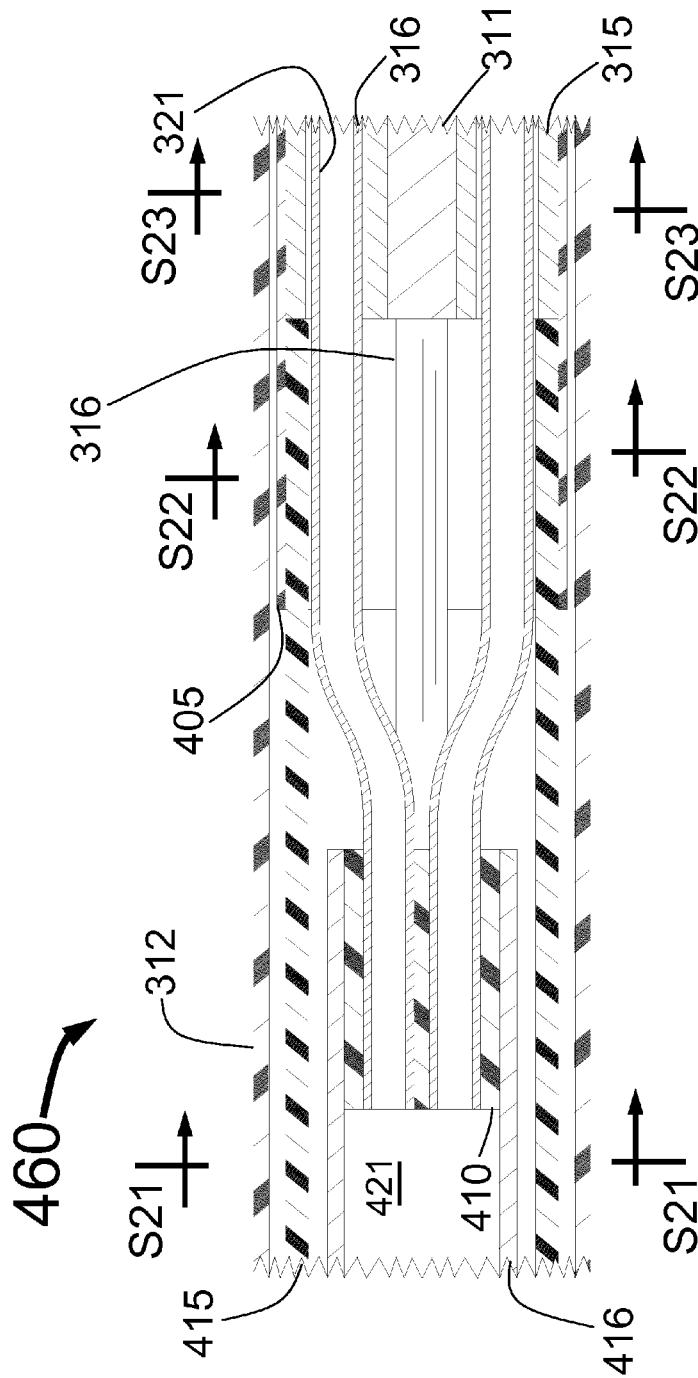


FIG. 20

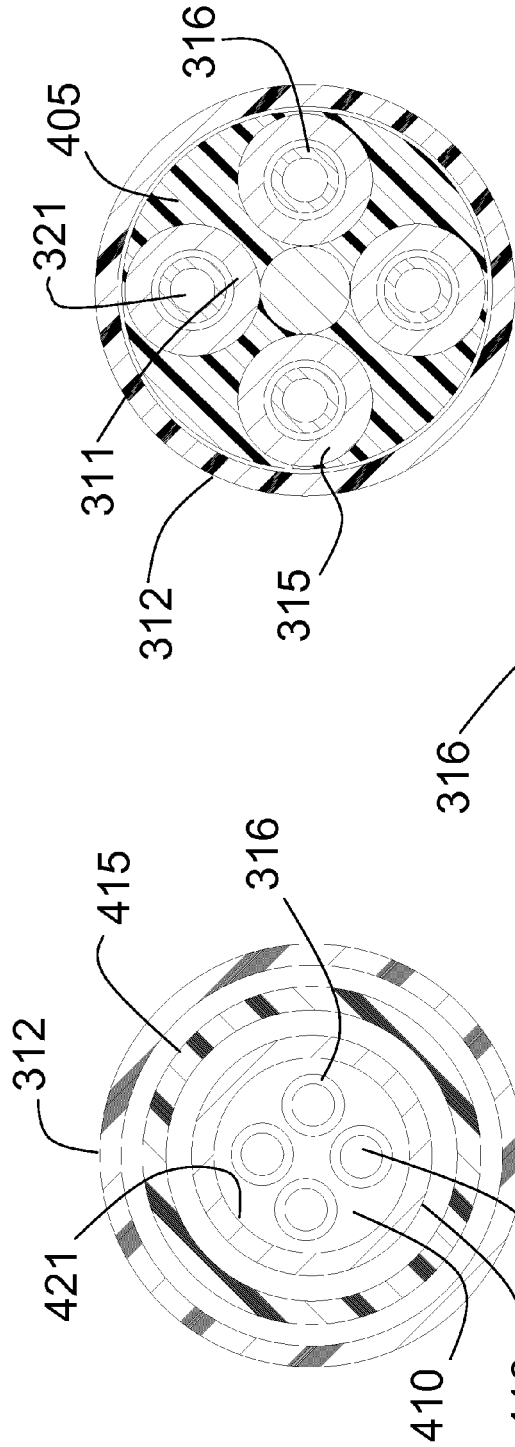


FIG. 21

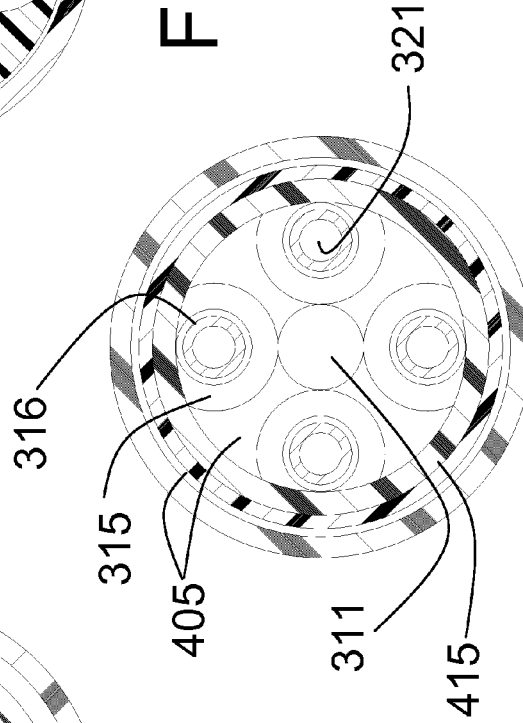


FIG. 22

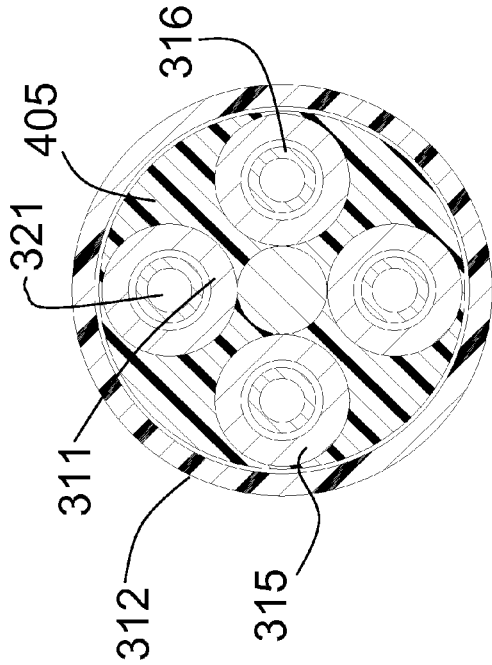


FIG. 23

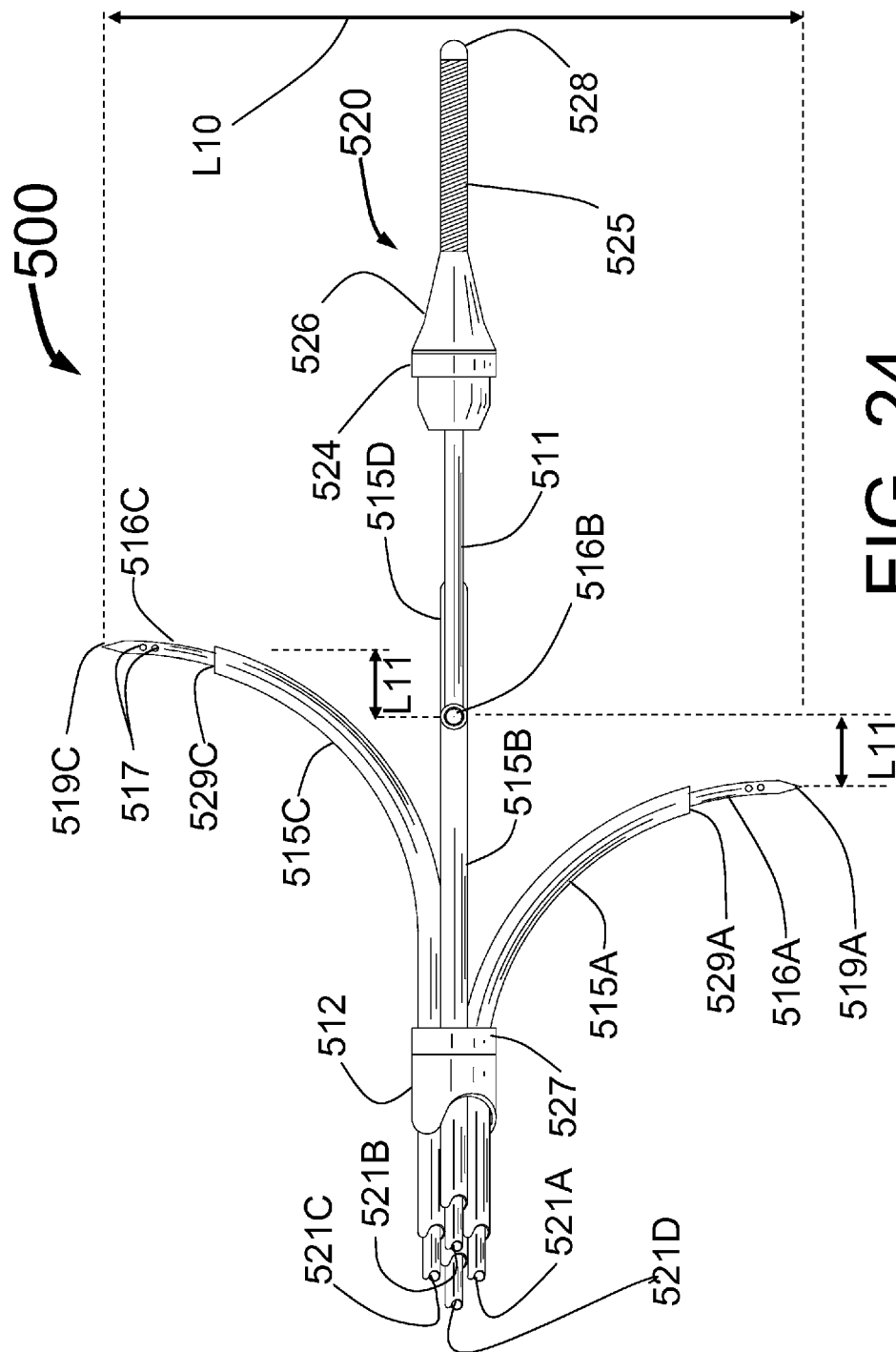


FIG. 24

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EXPANDABLE CATHETER SYSTEM FOR FLUID INJECTION INTO AND DEEP TO THE WALL OF A BLOOD VESSEL

REFERENCE TO RELATED APPLICATIONS

This Application is a Continuation-in-Part of patent application Ser. No. 13/216,495, filed 24 Aug. 2011, currently pending, and a Continuation-in-Part of patent application Ser. No. 13/294,439, filed 11 Nov. 2011, currently pending.

FIELD OF USE

This invention is in the field of devices to ablate muscle cells and nerve fibers for the treatment of cardiac arrhythmias, hypertension, congestive heart failure and other disorders.

BACKGROUND OF THE INVENTION

Since the 1930s it has been known that injury or ablation of the sympathetic nerves in or near the outer layers of the renal arteries can dramatically reduce high blood pressure. At the present time, physicians often treat patients with atrial fibrillation (AF) using radiofrequency (RF) catheter systems to ablate conducting tissue in the wall of the left atrium of the heart around the ostium of the pulmonary veins. Similar technology, using radiofrequency energy, has been successfully used inside the renal arteries to ablate sympathetic and other nerve fibers that run in the outer wall of the renal arteries, in order to treat high blood pressure. In both cases these are elaborate and expensive catheter systems that can cause thermal, cryoablative, or other methods to injure surrounding tissue. Many of these systems also require significant capital outlays for the reusable equipment that lies outside of the body, including RF generation systems and the fluid handling systems for cryoablative catheters.

Because of the similarities of anatomy, for the purposes of this disclosure, the term target wall will refer here to either the wall of the left atrium surrounding a pulmonary vein or the wall of a pulmonary vein near its ostium for AF ablation applications or the wall of the aorta around the ostium of the renal artery, or within the renal artery itself, for hypertension or congestive heart failure (CHF) applications.

In the case of atrial fibrillation ablation, the ablation of tissue surrounding multiple pulmonary veins can be technically challenging and very time consuming. This is particularly so if one uses RF catheters that can only ablate one focus at a time. There is also a failure rate using these types of catheters for atrial fibrillation ablation. The failures of the current approaches are related to the challenges in creating reproducible circumferential ablation of tissue around the ostium (peri-ostial) of a pulmonary vein. There are also significant safety issues with current technologies related to very long fluoroscopy and procedure times that lead to high levels of radiation exposure to both the patient and the operator, and may increase stroke risk in atrial fibrillation ablation.

There are also potential risks using the current technologies for RF ablation to create sympathetic nerve denervation from inside the renal artery for the treatment of hypertension or congestive heart failure. The short-term complications and the long-term sequelae of applying RF energy from inside the renal artery to the wall of the artery are not well defined. This type of energy applied within the renal artery, and with transmural renal artery injury, may lead to late restenosis, thrombosis, renal artery spasm, embolization of debris into the renal parenchyma, or other problems inside the renal artery. There may also be uneven or incomplete sympathetic nerve

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ablation, particularly if there are anatomic anomalies, or atherosclerotic or fibrotic disease inside the renal artery, such that there is non-homogeneous delivery of RF energy. This could lead to treatment failures, or the need for additional and dangerous levels of RF energy to ablate the nerves that run along the adventitial plane of the renal artery.

The currently used system for RF energy delivery also does not allow for efficient circumferential ablation of the renal sympathetic nerve fibers. If circumferential RF energy were applied in a ring segment from within the renal artery (energy applied at intimal surface to kill nerves in the outer adventitial layer) this could lead to even higher risks of renal artery stenosis from the circumferential and transmural thermal injury to the intima, media and adventitia. Finally, the "burning" or the inside of the renal artery using RF ablation can be extremely painful. Thus, there are numerous and substantial limitations of the current approach using RF-based renal sympathetic denervation.

The Bullfrog® micro infusion catheter described by Seward et al in U.S. Pat. Nos. 6,547,803 and 7,666,163 which uses an inflatable elastic balloon to expand a single needle against the wall of a blood vessel could be used for the injection of an chemical ablative solution such as alcohol but it would require multiple applications as it does not describe or anticipate the circumferential delivery of an ablative substance around the entire circumference of the vessel. The most number of needles shown by Seward is two and the two needle version of the Bullfrog® would be hard to miniaturize to fit through a small guiding catheter to be used in a renal artery. If only one needle is used, controlled and accurate rotation of any device at the end of a catheter is difficult at best and could be risky if the subsequent injections are not evenly spaced. This device also does not allow for a precise, controlled, and adjustable depth of delivery of a neuroablative agent. Another limitation of the Bullfrog® is that inflation of a balloon within the renal artery can induce stenosis due to balloon injury of the intima and media of the artery, as well as causing endothelial cell denudation.

Jacobson and Davis in U.S. Pat. No. 6,302,870 describe a catheter for medication injection into the inside wall of a blood vessel. While Jacobson includes the concept of multiple needles expanding outward, each with a hilt to limit penetration of the needle into the wall of the vessel, his design depends on rotation of the tube having the needle at its distal end to allow it to get into an outward curving shape. The hilt design shown of a small disk attached a short distance proximal to the needle distal end has a fixed diameter which will increase the total diameter of the device by at least twice the diameter of the hilt so that if the hilt is large enough in diameter to stop penetration of the needle, it will significantly add to the diameter of the device. For either the renal denervation or atrial fibrillation application, the length of the needed catheter would make control of such rotation difficult. In addition, the hilts which limit penetration are a fixed distance from the distal end of the needles. There is no built in adjustment on penetration depth which may be important if one wishes to selectively target a specific layer in the blood vessel or if one needs to penetrate all the way through to the volume past the adventitia in vessels with different wall thicknesses. Jacobson also does not envision use of the injection catheter for denervation. Finally, Jacobson in FIG. 3 when he shows a sheath over expandable needles, there is no guide wire and the sheath has an open distal end which makes advancement through the vascular system more difficult. Also the needles if they were withdrawn completely inside of the sheath they could because of the hilts, get stuck inside the sheath and be difficult to push out.

The prior art also does not envision use of anesthetic agents such as lidocaine which if injected first or in or together with an ablative solution can reduce or eliminate any pain associated with the denervation procedure.

Finally, while injection of ethanol as an ablative substance is well known and used within the heart and other parts of the body, there has been no development of an ethanol (or other liquid nerve ablation substances) injection system specifically designed for the circumferential ablation of sympathetic nerve fibers around the renal arteries.

SUMMARY OF THE INVENTION

The present invention, Intravascular Nerve Ablation System (INAS), is capable of applying an ablative fluid to produce circumferential damage in the nerve tissue that is in or near the wall of a blood vessel with a relatively short treatment time using a disposable catheter and requiring no additional capital equipment. The primary focus of use of INAS is in the treatment of cardiac arrhythmias, hypertension and congestive heart failure. Unlike the Bullfrog® or RF ablation devices that work with one or, at most two points of ablation, the present invention is designed to provide a more uniform circumferential injury to the nerves, while minimizing injury to the intima and medial layers of the vessel wall. The term circumferential delivery is defined here as at least three points of simultaneous injection of a suitable ablative solution within or just outside of a vessel wall, with the goal to ablate nerves completely around the circumference of a blood vessel. Circumferential delivery may be in a true circle or in a helical pattern so long as the entire 360 degrees or more is covered. Unlike the Jacobson device of U.S. Pat. No. 6,302,870, which does describe circumferential delivery, the present invention does not depend upon rotation of a tube to create outward movement nor does it have a fixed diameter hilt to limit penetration.

Specifically, there is a definite need for such a catheter system that is capable of highly efficient, and reproducible ablation of the nerves surrounding the renal artery ostium, or distal to the ostium in the renal artery wall, in order to damage the sympathetic nerve fibers that track from the peri-ostial aortic wall into the renal arteries, and thus improve the control and treatment of hypertension, etc.

This type of system may also have major advantages over other current technologies by allowing highly efficient, and reproducible circumferential ablation of the muscle fibers and conductive tissue in the left atrium, surrounding the ostium of the pulmonary veins or in the wall of the pulmonary veins near or at their ostium into the left atrium of the heart. Such ablation could interrupt atrial fibrillation (AF) and other cardiac arrhythmias. Other potential applications of this approach may evolve.

The present invention is a small (<2 mm diameter) catheter, which includes multiple expandable injector tubes, or guide tubes to allow passage of coaxial injector tubes, arranged circumferentially around the body of the INAS near its distal end. Each injector tube includes a needle at its distal end. Ablative fluid could be injected through the distal end of this needle which has injection egress through its distal end or through side holes placed just proximal to its distal end, needle has a (solid tipped) cutting distal end. There is a penetration limiting member as part of the INAS so that the needles will only penetrate into the tissue of the wall of the target blood vessel to a preset distance. These may be a preset distance proximal to the distal end of each needle similar to the hilts of the Jacobson et al patent or the penetration limiting member may be built into the proximal section of the INAS.

Limiting penetration is important to reduce the likelihood of perforation of the vessel wall, optimize the depth of injection or to adjust the depth to be into the volume just outside of the blood vessel wall. In a preferred embodiment for renal sympathetic nerve ablation, self-expanding guiding tubes are first deployed against the inside wall of the renal artery and act as a guide for separate coaxially longitudinally moveable injector tubes with sharpened needles with injection egress port(s) near the distal end.

The penetration limiting function of the present invention INAS as described herein uses one of the following techniques that will greatly reduce the diameter of the device as compared with the Jacobson designs of U.S. Pat. No. 6,302,870 and thus also improve the ability to deliver it into a vessel of a human body such as the renal artery. These techniques include:

Use of a cord or wire attached to the multiple needles that can fold during insertion to limit the diameter of the distal section of the INAS,

Use of one, two or more short NITINOL wires attached in the longitudinal direction at their proximal ends to the sides of the needle. The wires being designed to have their distal ends not be attached and having a memory state that curves away from the needle so as to act as a penetration limiting member for the needle. Such wires would fold tight against the needles to reduce the diameter of the distal section of the INAS,

Use of two bends in the needle the bend forming the penetration limiting member and the bend also being in the circumferential direction so as to not increase the diameter of the distal section of the INAS, and

Use of guide tubes that curve outward through which the needles slide in the longitudinal direction. The limit for penetration in this design is integral into the handles at the proximal end of the INAS and do not require diametric volume in the distal section of the INAS. This last embodiment has the added advantage of allowing adjustment of the penetration depth.

The injector tubes with distal needles are in fluid communication with an injection lumen in the catheter body, which is in fluid communication with an injection port at the proximal end of the INAS. Such an injection port would typically include a standard connector such as a Luer connector used to connect to a source of ablative fluid.

This injection system also anticipates the use of very small gauge needles (smaller than 25 gauge) to penetrate the arterial wall, such that the needle penetration could be safe, even if targeted to a plane or volume of tissue that is at, or deep to (beyond) the adventitial layer of the aorta, a pulmonary vein or renal artery. It is also anticipated that the distal needle could be a cutting needle rather than a coring needle and that the injection egress ports could be small injection holes (pores) cut into the sides of the injector tubes or distal needle, proximal to the cutting needle tip.

The expandable injector tubes or guide tubes may be self-expanding made of a springy material, a memory metal such as NITINOL or they may be made of a metal or plastic and expandable by other mechanical means. For example, the expandable legs with distal injection needles could be mounted to the outside of an expandable balloon whose diameter is controllable by the pressure used to inflate the balloon. There should be at least 2 injector tubes but 3 to 8 tubes may be more appropriate, depending on the diameter of the vessel to be treated. For example, in a 5 mm diameter renal artery, only 3 or 4 needles may be needed while in an 8 mm diameter renal one might need 6 needles.

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The entire INAS is designed to include a fixed distal guide wire or be advanced over a guide wire in either an over-the-wire configuration where the guide wire lumen runs the entire length of the INAS or a rapid exchange configuration where the guide wire exits the catheter body at least 10 cm distal to the proximal end of the INAS and runs outside of the catheter shaft for its proximal section. The fixed wire version is preferred as it would have the smallest distal diameter.

The INAS would also include a tubular, thin-walled sheath that constrains the self-expanding injection tubes with distal needles and/or guiding tubes prior to deployment, and for removal from the body. The sheath also allows the distal end of the INAS to be inserted into the proximal end of a guiding catheter or introducer sheath. The sheath also serves to protect the operator(s) from possible needle sticks and exposure to blood borne pathogens at the end of the procedure when the INAS is removed from the patient's body.

It is also envisioned that the injection needles, guiding tubes and injection tubes could be formed from a radiopaque material such as tantalum or tungsten or coated, or marked with a radiopaque material such as gold or platinum so as to make them clearly visible using fluoroscopy.

It is also envisioned that one or more of the injector needles could be electrically connected to the proximal end of the INAS so as to also act as a diagnostic electrode(s) for evaluation of the electrical activity in the area of the vessel wall.

It is also envisioned that one could attach 2 or more of the expandable legs to an electrical or RF source to deliver electric current or RF energy around the circumference of a target vessel to the ostial wall to perform tissue and/or nerve ablation.

It is also envisioned that this device could utilize one, or more than one neuroablative substances to be injected simultaneously, or in a sequence of injections, in order to optimize permanent sympathetic nerve disruption in a segment of the renal artery (neurotmesis). The anticipated neurotoxic agents that could be utilized includes but is not limited to ethanol, phenol, glycerol, local anesthetics in relatively high concentration (e.g., lidocaine, or other agents such as bupivacaine, tetracaine, benzocaine, etc.), anti-arrhythmic drugs that have neurotoxicity, botulinum toxin, guanethidine, heated fluids including heated saline, hypertonic saline, KCl or heated neuroablative substances such as those listed above.

The present invention also envisions use of anesthetic agents such as lydocaine which if injected first or in or together with an ablative solution can reduce or eliminate any pain associated with the denervation procedure.

The present invention also envisions use of a buffer before, after and/or between injections of contrast, anesthetic agents and/or neuroablative substances. For example, saline solution should be injected after the neuroablative substance for the first renal artery treated to make sure that all the neuroablative substance has been delivered and there is only saline in the injection lumen(s) and dead space of the INAS. Thus when the procedure begins on the second renal artery, contrast or an anesthetic agent can be delivered first to the desired location rather than having any residual ablative substance that is left in the INAS come out first. Ideally, once could envision the following sequence for injection using the INAS to ablate the sympathetic nerves in both renal arteries.

1. Flush the INAS out of the body with saline solution
2. Place the INAS and inject contrast to ensure that the injection egress points are properly located
3. Inject an anesthetic agent to prevent pain during ablation
4. Inject the neuroablative substance
5. Inject sufficient saline solution to flush all of the neuroablative substance from the INAS

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6. Close the INAS and retract the INAS back into the guiding catheter,
7. Access the other renal artery
8. Place the INAS and inject contrast to ensure that the injection egress points are properly located
9. Inject an anesthetic agent to prevent pain during ablation
10. Inject the neuroablative substance
11. Inject sufficient saline solution to flush all of the neuroablative substance from the INAS
12. Close the INAS and retract the INAS back into the guiding catheter,
13. Remove the INAS from the body

It is also envisioned that saline can be injected between steps 2 and 3, 3 and 4, 8 and 9 and/or 9 and 10.

It is also envisioned that one could utilize imaging techniques such as multislice CT scan, MRI or intravascular ultrasound imaging to get an exact measurement of the thickness and anatomy of the target vessel wall (e.g., renal artery) such that one could know and set the exact and correct penetration depth for the injection of the ablative agent prior to the advancement of the injector needles or injector tubes. The use of IVUS prior to use of the INAS may be particularly useful in order to target the exact depth intended for injection. This exact depth can then be targeted using the adjustable depth of penetration feature in our preferred embodiment(s). The selection of penetration depth can be accomplished using the proximal handles of the guide tube embodiment or by selection of an appropriate product code for the other designs that might have two to five versions each with a different penetration depth limit.

For use in the treatment of hypertension or CHF, via renal sympathetic nerve ablation, the present preferred embodiment of this invention INAS would be used with the following steps:

1. Engage a first renal artery with a guiding catheter placed through the femoral artery.
2. Advance the distal end of the INAS with a fixed distal guidewire into, and advance the INAS through the guiding catheter, until the distal end of the guiding tubes are passed beyond the distal end of the guiding catheter and into the renal artery.
3. Pull back the sheath allowing the expandable guide tubes to open up until the distal ends of the guide tubes press outward against the inside wall of the renal artery.
4. With the injector guide tubes having an outward curve or angle, the guide tube handle that controls the longitudinal motion of the guide tubes is then moved in the distal direction allowing the distal ends of the guide tubes that are touching the inside wall of the renal artery to further press against the intima and begin to flex backwards.
5. The guide tubes will then have their open distal ends facing into the renal artery wall. At this point contrast injection from the guiding catheter can confirm the correct spacing and position of the guide tubes.
6. Next, the injection tubes are be advanced coaxially through the guide tubes to an adjustable distance with a target of placing the injection egress to be at or just deep to the adventitial plane of the renal; artery. One or more penetrating limiting member(s) will allow the needles only to penetrate a preset distance (typically between 0.5 to 3 mm but preferably about 2-3 mm) into the vessel wall of the renal artery. Ideally, the very small gauge injection needles may be advanced to ~2-3 mm depth in the renal artery to deliver the neuroablative agent(s) at or deep to the adventitial plane, in order to minimize intimal and medial renal artery injury. The correct depth can be determined prior to the INAS treatment using CT

- scan, MRI or intravascular ultrasound to measure the renal artery wall thickness, such that the correct initial depth setting for the injector tube penetration is known prior to advancing the needles.
7. Attach an injection system, syringe or multiple syringes through a manifold to the connector at the INAS proximal end used to supply the ablative fluid. An anesthetic agent such as lidocaine can then be injected to eliminate or reduce any pain associated with the denervation procedure. The anesthetic agent can be injected before, after or at the same time as a small volume of contrast would be injected through the system, exiting at the injection egress near the distal end of the injector tubes to confirm the correct depth for injection of the neuroablative agent. Adjustment of the depth is possible at this time if the injection plane is determined to be too shallow (e.g., in media) or too deep (well outside the adventitial plane).
 8. Inject an appropriate volume of ethanol (ethyl alcohol), phenol, glycerol, lidocaine, bupivacaine, tetracaine, benzocaine, guanethidine, botulinum toxin or other appropriate neurotoxic fluid, including a combination of 2 or more neuroablative fluids or local anesthetic agents together or in sequence (local anesthetic first to diminish discomfort, followed by delivery of the ablative agent) and/or high temperature fluids (or steam), or extremely cold (cryoablative) fluid from the syringe or injection system through the catheter and out of the needles into the vessel wall and/or the volume just outside of the vessel. A typical injection would be 1-10 ml. This should produce a multiplicity of ablation zones (one for each injector tube) that will intersect to form an ablative ring around the circumference of the target vessel. Contrast could be added to the injection either during a test injection or during the therapeutic injection to allow x-ray visualization of the ablation zone.
 9. Once the injection is complete, retract the INAS injector tubes back inside the guide tubes. Then, retract and re-sheath the guide tubes by advancing the sheath over the guide tubes. This will collapse the guide tubes back under the sheath. The entire INAS can then be pulled back into the guiding catheter.
 10. In some cases, one may rotate the INAS 20-90 degrees and then repeat the injection if needed to make an even more definitive ring of ablation.
 11. The same methods as per prior steps can be repeated to ablate tissue in the contralateral renal artery.
 12. Remove the INAS from the guiding catheter completely.
 13. Remove all remaining apparatus from the body.
 14. A similar approach can be used with the INAS, via transeptal access into the left atrium to treat AF, via ablation of tissue in the vessel wall of one or more pulmonary veins. When indicated, advance appropriate diagnostic electrophysiology catheters to confirm that the ablation (in the case of atrial fibrillation) has been successful

It is also envisioned that one could mount injector tubes with needles on the outer surface of an expandable balloon on the INAS in order to deliver 2 or more needles into the vessel wall of a target vessel to inject ablative fluid.

Although the main embodiment of this invention utilizes two or more needle injection sites to circumferentially administer alcohol or other neuro-toxic fluid(s) to the wall of the renal artery for sympathetic nerve ablation, it is also envisioned that other modifications of this concept could also be utilized to achieve the same result. In one case it is envisioned that circumferential fluid based (ethanol or other ablative

fluid, a combination of ablative fluids, or heated fluid) could be administered in a circumferential fashion to a "ring segment" of the renal artery by injecting the ablative fluid into a space between two inflated balloons. Thus, after inflating a proximal occlusive balloon and a distal occlusive balloon, the ablative fluid would be injected into the space between the two balloons and allowed to dwell for a short period of time allowing the fluid, such as ethanol to penetrate through the arterial wall and reach the adventitial layer, thus disrupting and ablating the sympathetic nerves running in this space. After the dwell period the space could be flushed with saline and the balloons deflated.

Similarly, a single balloon with a smaller diameter near the middle of the balloon could function in the same way, as the ethanol or other ablative fluid, or a combination of ablative fluids, or heated fluid is injected in the "saddle-like" space in the central part of the balloon that is not touching the arterial wall.

It is also envisioned that another embodiment may include a circumferential band of polymer, hydrogel or other carrier, on the central portion of an inflatable balloon with the carrier containing the neurotoxic agent(s), such as alcohol, phenol, glycerol, lidocaine, bupivacaine, tetracaine, benzocaine, guanethidine, botulinum toxin, etc. The balloon would be inflated at relatively low pressure to oppose the intimal surface of the renal arterial wall, and inflated for a dwell time to allow penetration of the neurotoxic agent, circumferentially, into a "ring segment" of the renal artery and allow ablation of the sympathetic nerve fibers running near or in the adventitial plane.

It is also envisioned that the INAS catheter could be connected to a heated fluid, or steam, source to deliver high temperature fluids to ablate or injure the target tissue or nerves. The heated fluid could be normal saline, hypertonic saline, alcohol, phenol, lidocaine, or some other combination of fluids. Steam injection, of saline, hypertonic saline, ethanol, or distilled water or other fluids via the needles could also be performed in order to achieve thermal ablation of target tissue or nerves at and around the needle injection sites.

It is also envisioned that the INAS could utilize very small diameter needle injection tubes (e.g., 25-35 gauge) with sharpened needles at their distal ends such that the needles would be advanced to, or even through the adventitial plane of the renal artery or aortic wall using a penetration limiting member(s) or the combination of the guide tubes with an adjustable depth advancement of injector tubes through the guide tubes in order to set the depth of penetration, and allow one to "bathe" the adventitial layer containing the sympathetic nerves with neurotoxic fluid, while causing minimal injury to the intimal and medial vessel wall layers. These very tiny needles could pass transmurally through the arterial wall yet create such tiny holes in the arterial wall that blood leakage from the lumen to outside the vessel as well as medial layer injury would be minimal, and thus safe. Thus, the present invention could have the injection be either into the wall of the renal artery, into the adventitia of the renal artery or deep to the adventitial layer of the renal artery such that the injection needles or egress from injection tubes would occur via penetration all the way through the arterial wall to allow the ablative fluid to flow around and "bathe" the outside of the artery with one or more neuroablative substances.

Another embodiment may include two or more pores, or small metallic (very short) needle like projections on the outer surface of the central portion of an inflatable balloon, that would be in fluid communication with an injection lumen to allow injection into the wall of the renal artery and allow circumferential delivery of a neurotoxic agent(s). Given these

teachings and embodiment descriptions, other similar techniques could be envisioned to allow other variations upon this concept of a balloon expandable, circumferential ablation system for renal artery sympathetic nerve ablation.

Another embodiment of the present invention, as described in the methods above, places the means to limit penetration of the vessel wall at the proximal end of the INAS. In this embodiment, at least three guide tubes with expandable distal portions run along the distal portion of the length of the INAS. A guide tube handle with optional flushing port is attached to the proximal end of the INAS and controls the longitudinal motion of the guide tubes.

One injection tube is included for each guide tube where the injection tubes have sharpened (cutting needle) distal ends with injection egress ports just proximal to the cutting needle tip. The injection tubes are located coaxially inside of the guide tubes. The distal ends of the sharpened injection needles at the distal ends of the injection tubes are initially "parked" just proximal to the distal end of the guide tubes. A proximal injection tube handle attached to the proximal end of the injection tubes, or to the proximal end of a single injector tube that connects to the multiple injector tubes, is separated at its distal end from the proximal end of the guide tube handle forming a needle advancement gap. The injector tube handle has means to adjust the needle advancement gap distance. Alternately, the adjustment could be on the guide tube handle or a separate mechanism between the injector tube handle and guide tube handle. A fitting for injection of an ablative fluid is attached to the injector tube handle and is in fluid communication with the injection lumens of the injector tubes.

In its initial configuration a sheath lies outside of the guide tubes constraining them. The proximal end of the sheath is attached to a sheath handle which can be locked down to prevent longitudinal motion with respect to the guide tubes or unlocked to allow the sheath to be moved in the proximal or distal direction to open and close the INAS.

The process to use the INAS handles is to have each of the lumens in the INAS flushed with normal saline. The distal end of the INAS is then advanced through a guiding catheter into a vessel such as a renal artery. The sheath control handle is then pulled back holding the guide tube handle in position. This will allow the distal portion of the guide tubes to expand outwardly against the wall of a vessel such as a renal artery. Optionally, after the sheath is pulled back, the guide tubes can then be pushed slightly forward using the guide tube handle to ensure they are engaged firmly against the vessel wall. The injector tube handle is then advanced so as to push the distal ends of the injection tubes having sharpened injection needles out of the distal end of the guide tubes which are touching the inside of the vessel wall. The needles will penetrate into the media of the vessel wall. Depending on the advancement gap, the penetration of the needles into the vessel wall can be limited. This can permit selective injection through the injection egress ports of the needles into the media, adventitia, outside of the adventitia or any combination of these depending on the number and location of injection egress ports. After the needles are properly placed into or through the vessel wall, a source of ablative fluid such as ethanol is attached to the fitting in the injection tube handle and the fluid is injected through the lumens inside the injector tubes and out through the injection egress ports into the tissue.

After the injection is complete, the injection tube handle is pulled back to retract the needles into the distal portion of the guide tubes. The sheath control handle is then advanced to collapse the guide tubes and close the INAS. The sheath control handle is then locked down to prevent inadvertent

opening of the INAS. The INAS is then pulled back onto the guiding catheter and the same procedure can be repeated for the other renal artery.

Although it is envisioned that there could be a number from one to 8 injector tubes inside of 8 guide tubes, it is likely that 3 or 4 tubes is optimal for circumferential tissue ablation.

While complete circular ablation of the sympathetic nerves around the outside of a renal artery will be very effective in reducing blood pressure, it may be desirable to longitudinally offset the injection points to create a helical (spiral) ablation pattern that will still completely ablate the sympathetic nerves in the outer layers of each renal artery while reducing the damage to the artery circumferentially at a single location. Thus an embodiment of the present invention is envisioned where each successive injection egress point is longitudinally offset from adjacent egress points.

While the examples of use of the present invention disclosed herein are focused on renal denervation, it is envisioned that the present invention fluid injection system can be used for any application where injection into the wall of a blood vessel or beyond (deep to) the wall of a blood vessel is desired. Examples include injection of a cytostatic substance such as sirolimus for preventing arterial restenosis, and injection of a chemotherapy drug into or beyond the hepatic artery for treatment of liver cancer.

Thus it is an object of the present invention INAS is to have a percutaneously delivered catheter that can be used to treat atrial fibrillation with one, or more injections of an ablative fluid into the vessel walls of the pulmonary veins near the ostium, or into the left atrial tissue surrounding one or more of the pulmonary veins.

Another object of the present invention INAS is to have a percutaneously delivered catheter that can be used to treat hypertension with one, or more injections of an ablative fluid into or deep to, the vessel wall of the renal arteries, or into the wall of the aorta surrounding the ostium of the renal artery.

Another object of the present invention INAS is to facilitate injection of an ablative fluid into or beyond the outer layers of the renal artery to reduce or prevent injury to the inner layers including the media of the renal artery.

Still another object of the present invention INAS is to have a percutaneously delivered catheter that includes a multiplicity of circumferentially expandable injector tubes, each tube having a needle at its distal end with injection egress allowing the delivery of an ablative fluid into the wall of a target vessel or into the space beyond the vessel wall.

Still another object of the invention is to have a flexible penetration limiting member or means attached just proximal to the distal end of each injector needle, or relatively blunt tipped guiding tubes to limit the depth of needle penetration into, or just through, the vessel wall.

Still another object of the present invention is to have a sheath that in conjunction with a distal tip provide for open and closed positions of the INAS. The closed position has the sheath and distal tip touching so as to totally enclose the sharpened needles while the open position allows the needles to expand outward for injection of the ablative fluid into or deep to the vessel wall.

Yet another object of the present invention is to use heated or cooled ablative fluid to be the source of the tissue ablation such as with heated or cooled normal saline or enhance the efficacy of an already ablative fluid such as ethanol.

Yet another object of the present invention INAS is to have one or more of the injector needles act as diagnostic electrodes for measurement of electrical activity within the wall of the target vessel.

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Yet another object of this invention is to use a multiplicity of coaxially guided injector tubes that move slidably within corresponding expandable guiding tubes, to allow the safe, controlled and adjustable depth of passage of injector tubes with sharpened needles at their distal ends into and/or through the wall of a target vessel, to allow controlled chemoablation of nerves in the adventitial layer of an artery while minimizing intimal and medial injury of said artery.

Yet another object of the present invention is to provide injection of an anesthetic agent before or during injection of the ablative fluid so as to prevent or reduce any pain associated with the denervation procedure.

Yet another object of the present invention is to provide injection egress points that form a helical pattern which will still provide ablation of all fibers of the sympathetic nerves in the outer layers of a renal artery with less risk of circumferential damage to the artery, thus potentially reducing the risk of negative (arterial) remodeling.

These and other objects and advantages of this invention will become obvious to a person of ordinary skill in this art upon reading of the detailed description of this invention including the associated drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a longitudinal cross section drawing of the distal portion of the present invention Vascular Nerve Ablation System (INAS) having a fixed guide wire at its distal end.

FIG. 2 is a schematic view of the distal portion of the INAS in its closed position as it would be configured for delivery into the human body or to cover the injector needles during removal from the human body.

FIG. 3 is a schematic view of the distal portion of the INAS in its open position as it would be configured for delivery of an ablative solution into the target vessel wall.

FIG. 4 is a longitudinal cross sectional drawing of the proximal end of the fixed wire embodiment of the INAS of FIGS. 1 through 3.

FIG. 5A is a schematic view of the distal portion of the closed INAS of FIG. 2 as it is first advanced out of a guiding catheter into a renal artery.

FIG. 5B is a schematic view of the distal portion of the closed INAS as the sheath is being pulled back to allow the expandable tubes open against the wall of the renal artery distal to the ostium.

FIG. 5C is a schematic view of the distal portion of the fully open INAS of FIG. 3 with needles fully embedded into the wall of the renal artery to allow the infusion of an ablative substance into the vessel wall.

FIG. 5D is a schematic view of the distal portion of the closed INAS as the distal portion of the INAS is being pulled back into the sheath to close the INAS either for subsequent use in the other renal artery or for removal from the body.

FIG. 5E is a schematic view of the distal portion of the closed INAS of FIG. 2 after it has been closed by retraction of the distal portion of the INAS into the sheath either for subsequent use in the other renal artery or for removal from the body.

FIG. 6 is a longitudinal cross section drawing of the embodiment of the INAS that is delivered over a separate guide wire.

FIG. 7 is a longitudinal cross sectional drawing of the proximal end of an over-the-wire embodiment of the INAS of FIG. 6.

FIG. 8 is a longitudinal cross section drawing of an injector capable of delivering a heated ablative solution into the INAS of FIGS. 1-4.

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FIG. 9 is a longitudinal cross section drawing of the proximal section of an injection needle showing longitudinal welded wire penetration limiting members.

FIG. 10 is a schematic view of the proximal section of another embodiment of the present invention that delivers an ablative fluid circumferentially to the inside of a target vessel.

FIG. 11 is a longitudinal cross section of another embodiment of the present invention INAS in its closed position having four injector tubes that can slide within four guide tubes. The injector tubes have sharpened needles having injection egress ports at the distal end of each injector tubes.

FIG. 12 is an enlargement of the area S12 of FIG. 11 showing the distal portion of the injector tubes and guide tubes.

FIG. 13 is a circumferential cross section at S13-S13 of the INAS of FIG. 11.

FIG. 14 is a longitudinal cross section of the expanded distal portion of the INAS.

FIG. 15 is an enlargement of the area S15 of FIG. 14.

FIG. 16 is a longitudinal cross section of the proximal end of the INAS of FIGS. 11-15.

FIG. 17 is an enlargement of the area S17 of FIG. 16.

FIG. 18 is an enlargement of the area S18 of FIG. 16.

FIG. 19 is a longitudinal cross section of an alternate embodiment of all but the distal portion of the INAS using multiple guide tubes.

FIG. 20 is a longitudinal cross section of a central transition portion connecting the proximal portion of the of the INAS of FIG. 19 with the distal portion of the INAS of FIGS. 11-14.

FIG. 21 is a circumferential cross section at S21-S21 of the INAS central transition portion of FIG. 20.

FIG. 22 is a circumferential cross section at S22-S22 of the INAS central transition portion of FIG. 20.

FIG. 23 is a circumferential cross section at S23-S23 of the INAS central transition portion of FIG. 20.

FIG. 24 is a schematic view of the distal portion of another embodiment of the INAS having longitudinally offset injection egress locations to allow helical (spiral) chemical nerve ablation.

DETAILED DESCRIPTION OF THE DRAWINGS

FIG. 1 is a longitudinal cross section drawing of the distal portion of the present invention Vascular Nerve Ablation System (INAS) 10 having a fixed guide wire 25 with tip 28 at its distal end. FIG. 1 shows the INAS 10 in its fully open position with the self-expanding injector tubes 15 with distal ends sharpened to form injection needles 19 open to their maximum diameter. Flexible cords 13 with adhesive 14 that attaches the cords 13 to the injector tubes 15 act as a penetration limiting member to prevent the distal tip of the needles 19 from penetrating more than a maximum distance L into a vessel wall. The injector tubes can be made from any springy material with the preferred material being NITINOL. A separate spring or inflatable balloon could be placed inside of the injector tubes if the tubes are self-expanding to achieve the same objective. A balloon while increasing the diameter of the system would be able to push the needles with great force into the vessel wall.

A sheath 12 with radiopaque marker 27 is shown in FIG. 1 in its position where it has been pulled back to allow full expansion of the injector tubes 15. There are 4 injector tubes 15 in this embodiment of the INAS 10 although as few as 2 and as many as 12 are envisioned. The distance L can be between 0.2 and 2 mm with the optimal being about 1 mm.

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The distal section 20 of the INAS 10 includes the distal wire 25, tapered flexible tip 26, radiopaque marker 24 and sheath engagement section 22 that assures that the distal portion of the INAS 10 will properly pull back into the sheath 12 following use of the INAS 10 to ablate tissue in a vessel of the human body. The INAS 10 is fully closed when the two radiopaque markers 27 and 24 are next to each other. This provides a visual indication during fluoroscopy.

The proximal end of the injector tubes 15 are held by a manifold 17 that is attached inside the distal end of the outer tube 16 and the core wire 11. The proximal end of the outer tube 16 is attached to a hypotube 18 that continues to the proximal end of the INAS 10. The hypotube 18 is typically made from a metal like 316 Stainless steel and the outer tube 16 is made from a plastic or metal reinforced plastic so that it is flexible enough to allow the INAS to easily be advanced and retracted around the bend in a typical guiding catheter such as that used for angioplasty or stenting of the renal arteries. The outer tube 16 would typically be between 5 and 30 cm long although it is also envisioned that the INAS 10 could be designed without a hypotube 18 and only a plastic or metal reinforced plastic outer tube 16 running to the proximal end.

The core wire 11 is attached to the inside of the hypotube 18 at junction point 23. This attachment could for example be by adhesive means, welding or brazing. Spot welding is the preferred method. In this way, the core wire 11 that supports the fixed wire 25 cannot be easily detached from the INAS 10. The injector lumen 21 inside of the hypotube 18 connects to the lumen of the outer tube 16 which is in fluid communication with the injector tube lumens 29 of each of the expandable tubes 15 allowing an ablative substance or solution to flow from the proximal end of the INAS 10 through the hypotube 18, through the outer tube 16, through the expandable injector tubes 15 and out of the sharpened injector needles 19 into a vessel wall.

FIG. 2 is a schematic view of the distal portion of the INAS 10' in its closed position as it would be configured for delivery into the human body or to cover the injection needles 19 during removal from the human body. The INAS 10' includes fixed wire 25 with tip 28, core wire 11, outer tube 16 and sheath 12. In this configuration the two radiopaque markers 27 and 24 are adjacent to each other with the sheath 12 being advanced to it fully distal position. Of great importance in this design is that in the closed position, the sharpened needles 19 are completely enclosed by the sheath 12 which is closed over the proximal portion of the tapered tip 26.

FIG. 3 is a schematic view of the distal portion of the present invention Intravascular Nerve Ablation System (INAS) 10 in its fully open position having a fixed guide wire 25 with tip 28 at its distal end. FIG. 3 shows the INAS 10 in its fully open position with the self-expanding injector tubes 15 with distal ends sharpened to form injection needles 19 open to their maximum diameter. Flexible cords 13 with adhesive 14 that attaches the cords 13 to the injector tubes 15 act as a penetration limiting member to prevent the distal tip of the needles 19 from penetrating more than a maximum distance L shown in FIGS. 1 and 3 into a vessel wall.

A sheath 12 with radiopaque marker 27 is shown in FIG. 3 in its position where it has been pulled back to allow full expansion of the injector tubes 15. There are 4 injector tubes 15 in this embodiment of the INAS. The distal section 20 of the INAS 10 includes the fixed distal wire 25, tapered flexible tip 26, radiopaque marker 24 and sheath engagement section 22 that assures that the distal portion will properly pull back into the sheath 12 following use of the INAS 10 to ablate tissue in a vessel of the human body. Also shown in FIG. 3 are the outer tube 16 with injection lumen 21 and core wire

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FIG. 4 is a longitudinal cross sectional drawing of the proximal end of the fixed wire embodiment of the INAS 10 of FIGS. 1 through 3. The hypotube 18 with injection lumen 21 also shown in FIG. 1, has a Luer fitting 35 with lumen 36 attached to its proximal end allowing a source of an ablative substance of solution to be injected through the lumen 36 of the Luer fitting 35 into the lumen 21 of the hypotube 18 and subsequently out of the injection needles 19 of FIGS. 1 through 3. The proximal end of the sheath 12 is attached to the distal end of the Tuohy-Borst fitting 30 with handle, 36, inner hub 33 washer 39 and O-Ring 43. As the handle 36 is tightened by screwing it down over the inner hub 33, the O-Ring will compress sealing the Tuohy-Borst fitting 30 against the hypotube 18. A side tube 31 with Luer fitting 32 having a lumen 34 is designed to allow the lumen 38 between the inside of the sheath 12 and hypotube 18 to be flushed with saline before insertion of the INAS 10 into a human body. Before insertion into the body, the Tuohy-Borst fitting 30 is tightened onto the hypotube 18 with the sheath 12 in its most distal position and the INAS 10' closed as is shown in FIG. 2. When in the distal end of the INAS 10' is properly positioned in one of the renal arteries, the Tuohy-Borst fitting is loosened and the handle 36 is pulled in the proximal direction while the Luer fitting 35 is held in place. This will open the INAS 10 and allow the injector tubes 15 of FIG. 1 to expand outward in the vessel.

FIG. 5A is a schematic view of the distal portion of the closed INAS 10' of FIG. 2 as it is first advanced out of a guiding catheter 80 into a renal artery just distal to the ostium with the aorta. The INAS 10' is advanced until the marker band 24 distal to the distal end of the guiding catheter 80. It is anticipated that an optimal distance of 5 to 15 mm distal would work best although shorter and longer distances are possible depending on the geometry of the renal artery and the distance of penetration of the guiding catheter 80 into the ostium of the renal artery.

FIG. 5B is a schematic view of the distal portion of the closed INAS 10" as the sheath 12 is being pulled back to allow the expandable tubes 15 open against the wall of the renal artery just distal to the ostium into the aorta. In this position, it is desired that the angle A at which the distal end of the injection needles engage the inside of the vessel wall should be less than 80 degrees and ideally between 40 and 60 degrees. If the angle is too large, the injection tubes could buckle backwards instead of pushing the sharpened needles into the vessel wall. If the angle is too small, the needles might not penetrate properly and might slide distally along the inside of the vessel wall. After the sheath 12 is pulled back so it no longer constrains the expandable injector tubes 15, the INAS 10" is then pushed in the distal direction allowing the injector tubes 15 to continue their outward expansion as the injection needles 19 penetrate into the wall of the renal artery. The penetration will stop when the cords 13 engage the wall of the renal artery limiting the penetration of the needles 19. Alternatively, this "cord" may be replaced by a nitinol wire structure that is fixably attached to the injector tubes 15 to provide a (stiffer) metallic penetration limiting member.

FIG. 5C is a schematic view of the distal portion of the fully open INAS 10 of FIG. 3 with needles 19 fully embedded into the wall of the renal artery to allow the infusion of an ablative substance into the vessel wall. Although FIG. 5C shows the cords 13 fully expanded, it would be typical for them to be slightly less in diameter than their maximum diameter when they engage the wall of the renal artery to limit the penetration of the needles 19. Preferably, the maximum diameter of the INAS 10 system selected for the procedure should be at least 2 to 4 mm greater than the inside diameter of the renal artery.

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For example, if the renal artery diameter at the desired ablation site is 5 mm in diameter, then a INAS 10 with maximum diameter of 7 to 9 mm should be selected. In the configuration of FIG. 5C, the ablative substance is injected through the needles 19 into the wall of the renal artery. The preferred ablative substance is ethyl alcohol (ethanol), which has historically been used to ablate tissue, particularly nerve tissue in the cardiovascular system. Other agents such as phenol, glycerol, local anesthetic agent(s) such as lidocaine, guenethidine or other cytotoxic and/or neurotoxic agents are also anticipated as possible injectates.

FIG. 5D is a schematic view of the distal portion of the closed INAS 10" as its distal portion is being pulled back into the sheath 12 to close the INAS 10" either for subsequent use in the other renal artery or for removal from the body. A shaded area shows the ablated region 100 where the tissue in the wall of the renal artery has been ablated. If the needle depth of penetration is set at a greater depth (e.g. 2.5-3 mm) the ablation zone may be deeper (primarily adventitial) and create less injury to the intimal and medial layers of the renal artery wall than is shown in 5D.

FIG. 5E is a schematic view of the distal portion of the closed INAS 10' of FIG. 2 after it has been closed by retraction of the distal portion of the INAS into the sheath 12 either for subsequent use in the other renal artery or for removal from the body.

For this embodiment of the INAS 10, the method of use for hypertension would be the following steps:

1. Remove the sterilized INAS 10 from its packaging in a sterile field, flush the lumen 38 between the outer tube 12 and hypotube 18 with saline.
2. Advance the sheath 12 until the INAS 10' is in its close position.
3. Lock the Tuohy-Borst fitting 30 down onto the hypotube 18 of FIG. 4.
4. Access the aorta via a femoral artery, typically with the insertion of an introducer sheath.
5. Using a guiding catheter 80 of FIGS. 5A through 5E or a guiding sheath with a shaped distal end, engage the first targeted renal artery through the aorta. This can be confirmed with contrast injections as needed.
6. Place the distal end of the INAS 10 in its closed position of FIG. 2 into the proximal end of the guiding catheter 80. There is typically a Tuohy-Borst fitting attached to the distal end of a guiding catheter 80 to constrain blood loss.
7. The closed INAS 10 can be pushed through the opened Tuohy-Borst fitting into the guiding catheter 80.
8. Advance the INAS 10 through the guiding catheter, until the marker band 24 is distal to the distal end of the guiding catheter within the renal artery as shown in FIG. 5A.
9. Pull the sheath 12 back in the proximal direction while holding the Luer fitting 35 and hypotube 18 the proximal end of the INAS 10 fixed. This will allow expansion of the injector tubes 15 against the wall of the renal artery as shown in FIG. 5B.
10. Lock the Tuohy-Borst fitting 30 down on the hypotube 18.
11. With the Tuohy-Borst fitting at the proximal end of the guiding catheter 80 loosened advance the sheath 12 and hypotube 18 locked together pushing the sharpened needles 19 into, or through, the wall of the renal artery as the self-expanding injector tubes 15 continue to expand outward. The injector tubes 15 will stop penetration when penetration limiting member 13 engages the wall

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of the renal artery thus limiting the penetration of the needles 19 to the desired depth.

12. Attach a syringe or injection system to the Luer fitting 35 of FIG. 4 that provides ablative fluid that will be injected into the wall of the renal artery

13. Inject an appropriate volume of ethanol (ethyl alcohol) or other appropriate cytotoxic fluid, or combination of neuroablative fluids, or heated fluid or steam (e.g., 90-95 degree heated saline solution) from the syringe or injection system through the lumen 36 and out of the needles 19 into the wall of the renal artery. A typical injection would be 1-10 ml. This should produce a multiplicity of intersecting volumes of ablation (one for each needle) that should create a torroid of ablated tissue around the circumference of the renal artery as shown as the ablated regions shown in FIGS. 5D and 5E. Contrast and/or an anesthetic agent such as lidocaine can be injected before or at the same time as the ablative fluid.

14. Loosen the Tuohy-Borst fitting 30 and while holding the Tuohy-Borst fitting 30 and sheath 12 fixed, pull the Luer 35 with hypotube 18 in the proximal direction until the expandable tubes 15 with needles 19 are fully retracted back into the distal end of the sheath 12 and the marker bands 27 and 25 are next to one another. This is shown in FIGS. 5D and 5E.

15. In some cases, one may advance the INAS 10 again into the renal artery, rotate it between 20-90 degrees and then repeat the injection to make an even more definitive volume of ablation. This would be advantageous if the INAS 10 has fewer than 4 injector tubes and should not be needed with the 4 injector tubes shown in herein.

16. The same methods as per steps 8-15 can be repeated to ablate tissue around the other renal artery during the same procedure.

17. Remove the INAS 10 in its closed position from the guiding catheter. Being in the closed position, the needles 19 are enclosed and cannot harm the health care workers, or expose them to blood borne pathogens.

18. Remove all remaining apparatus from the body.

A similar approach can be used with the INAS 10, to treat atrial fibrillation through a guiding catheter inserted through the septum into the left atrium with the wall of the target vessel being the wall of one of the pulmonary veins.

FIG. 6 is a longitudinal cross section drawing of the distal portion of another embodiment the present invention Vascular Nerve Ablation System (INAS) 40 that is delivered over a separate guide wire 60. FIG. 6 shows the INAS 40 in its fully open position with the self-expanding injector tubes 45 with distal ends sharpened to form needles 49 open to their maximum diameter. Flexible cords 43 connect the injector tube 45 and act as a penetration limiting member to prevent the distal tip of the needles 49 from penetrating more than a maximum distance D into a vessel wall. Unlike the cord 13 of FIG. 1, the cords 43 are fed through holes 57 in the sides of each injector tube 45 a distance D from the distal end. A drop of adhesive (not shown) can be used to seal the holes and prevent leakage of the ablative substance or solution during injection into a vessel wall.

A sheath 42 is shown in its position where it has been pulled back to allow full expansion of the injector tubes 45. There are 4 injector tubes 45 in this embodiment of the INAS 40 although as few as 2 and as many as 12 are envisioned. The distance D can be between 0.2 and 2 mm with the optimal being about 0.5-1 mm.

The proximal end of the injector tubes 45 are held by a manifold 47 that is attached inside the distal end of the outer tube 46 and the inner tube 48. An injection lumen 51 lies

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between the inner tube 48 and outer tube 46 proximal to the manifold 47. Ablative material injected through the injection lumen 51 will flow into the proximal ends of the injector tubes 45 and then out of the injection needles 49 into one or more layers of the blood vessel and/or into the volume of tissue just outside the vessel wall.

The distal section 50 of the INAS 40 that is coaxially attached to the distal section of the inner tube 48 includes the tapered flexible tip 56, radiopaque marker 55 and sheath engagement section 54 that assures that the distal portion of the INAS 40 will properly pull back into the sheath 42 following use of the INAS 40 to ablate tissue in a vessel of the human body. The guide wire 60 can be advanced and retracted in the longitudinal direction inside of the guide wire lumen 41 that lies inside of the inner tube 48. The INAS 40 can be configured either as an over-the-wire or a rapid exchange device. If over-the-wire, the guide wire lumen 41 inside of the inner tube 48 runs all the way to the proximal end of the INAS 40 as is shown in FIG. 7. If a rapid exchange configuration is used then the guide wire would exit from the INAS 40 and run external to the outside of the INAS 40 for some portion of the length of the INAS 40. If a rapid exchange is used then a slot will be needed in the sheath 42 to allow for the sheath 42 to move longitudinally with respect to the rest of the INAS 40. The proximal end of the rapid exchange configuration would be identical to that of the fixed wire INAS 10 of FIG. 4. The guide wire would typically run outside of the body of the INAS 40 for at least the most proximal 10 cm with the preferred embodiment having the guide wire exit through the side of the outer tube 46 and sheath 42 between 5 and 15 cm from the distal end of the INAS 40.

FIG. 7 is a longitudinal cross sectional drawing of the proximal end 70 of an over-the-wire embodiment of the INAS 40 of FIG. 6. The inner tube 48 has a Luer fitting 78 attached to its proximal end. The guide wire 60 can be advanced through the guide wire lumen 41 inside of the inner tube 48. The proximal end of the outer tube 46 is attached to the hub 79 that is sealed against the inner tube 48, forming the injection lumen 51 between the inner tube 48 and outer tube 46. A side tube 74 with lumen 76 connects into the hub 79 with a Luer fitting 75 attached to the proximal end of the side tube 74. A syringe or other injection device can be attached to the Luer fitting 75 to inject an ablative substance or solution through the lumen 76 into the injection lumen 51 into the injector tube 45 of FIG. 6 and out of the ends of the injection needles 49 into a vessel wall. The proximal end of the sheath 42 connects to the hub 77 that acts as a handle to slide the sheath 42 coaxially over the outer tube 46 to open and close the INAS 40 of FIG. 6. A side tube 72 with lumen 73 connects into the hub 77. A Luer fitting 71 is attached to the proximal end of the side tube 72 to allow the lumen 62 between the sheath 42 and the outer tube 46 to be flushed with saline solution before introduction of the INAS 40 in to the human body. While the hub 77 shown here is a plastic member, it is envisioned that a Tuohy-Borst fitting such as the Tuohy-Borst fitting 30 of FIG. 4 could be used here and could be advantageous as it would allow one to lock the sheath 42 in position onto the outer tube 46 during insertion and removal from the body so that the distal end of the sheath 42 would remain in its most distal position protecting the injection needles 49 and protecting health care workers from exposure to needle stick injury.

FIG. 8 is a longitudinal cross section of a disposable injector 90 for use in providing ablative fluid heated to a preset temperature for injection through the INAS 10 of FIGS. 1-5C to ablate tissue in a human body. The injector 90 includes a syringe 104 with fluid storage volume 99 and female Luer fitting 93 that would typically attach to a standard stopcock

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(not shown) the stopcock being connected to the male Luer fitting 35 at the proximal end of the INAS 10 of FIGS. 1-4. It is also envisioned that a stopcock could be provided with either the injector 90 or INAS 10 or integrated into either. The syringe 104 is surrounded by the heating coil 94 which is contained within the case 95 filled with heat insulation 96. The power for the heating coil 94 comes from the battery 98 with positive terminal 91 and negative terminal 92 housed in the battery case 97. A moveable plunger 101 with handle 102 and distal sealing gasket 103 is used to inject the heated ablative fluid in the volume 99 through the Luer fitting 93 into the INAS 10 injector lumen 21 of FIG. 4 where it will then flow out through the injector needles 19 of FIGS. 1 and 3 into the tissue as shown in FIG. 5C. The injector 90 may include closed loop electronics with either a display of the temperature or one or more LEDs that let the user know when the ablative fluid in the syringe 104 is at the desired temperature. The injector 90 could be manufactured for a single preset temperature or be adjustable to more than one temperature. While FIG. 8 shows a manual injection plunger 101, it is also envisioned that a fluid pump or mechanical system to depress the plunger could be integrated into the injector 90. The use of heated fluid to ablate tissue may be either effective by having a normally benign substance like normal saline heated to the point where the heat causes the tissue ablation or the heat may act to improve the ablative ability of a fluid such as alcohol that is normally ablative at room or body temperature.

FIG. 9 is a longitudinal cross section drawing of the proximal section of an injection needle 110 with lumen 111 and distal end 119, showing attached longitudinal memory metal wire penetration limiting members 114 and 116 with proximal portions 112 and 113 respectively. These proximal portions 112 and 113 are attached (glued, welded or brazed) to the outside 115 of the needle so that when the needles 110 are released from inside of the sheath 12 of FIGS. 1-4 the distal portion of the wires 114 and 116 will assume their memory state as shown in FIG. 9 forming a member that will limit penetration of the needle tip 119 to approximately a preset distance L2. Since most arteries have a similar thickness, the distance L2 can be set to ensure the ablative fluid injected through the needle lumen 111 will emerge in the appropriate volume of tissue. Selection of the appropriate volume can be set by different values of L2 such that the injection can be set to be in the media of the artery, the adventitia of the artery or outside the adventitia of the artery. While FIG. 9 shows two wires 114 and 116, one wire would also function to limit penetration or 3 or more wires could also be used. Ideally the wire(s) would be attached to the outside of the needle 115 on the sides circumferentially of the needle and not on the inside or outside where the wires 114 and 116 would increase the diameter of the closed INAS 10 of FIGS. 1-4 before the sheath 12 is pulled back to deploy the needles.

It is also envisioned that an injector designed to deliver a super-cooled ablative fluid into the INAS of FIGS. 1-4 could also be appropriate for this application.

An important aspect of the present invention is the circumferential delivery of the ablative fluid with respect to the vessel wall. Such delivery from one or more injection egress points must attack the nerve tissue circumferentially and at the correct depth to ensure efficacy, and ideally to minimize injury to the healthy and normal cellular structures of the intimal and medial layers. The circumferential delivery in a circular or helical pattern can be handled as described above in three different ways.

1. Injection into the vessel wall at three or more points around the circumference of the vessel

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2. Injection into the space outside of wall of the vessel—although this can be accomplished by a single needle/egress point, this is best done with at least two egress points so that the needles can be kept small so as to allow the vessel wall to reseal as the needles are retracted.
3. Injection into the inside to fill an annular space and delivery the ablative fluid circumferentially to the inside surface of the vessel.

FIG. 10 is a schematic view of yet another embodiment of the distal portion of the present invention Intravascular Nerve Ablation System (INAS) 200 in its fully open position having a fixed guide wire 225 with tip 228 at its distal end. FIG. 10 shows the INAS 200 in its fully open position with the self-expanding injector tubes 215 with distal ends sharpened to form injection needles 219 open to their maximum diameter. In this embodiment the injector tubes 215 each have a double bend or kink 214 having length L4 in the circumferential direction. The kinks 214 act as a penetration limiting member to prevent the distal tip of the needles 219 from penetrating more than a maximum distance L3 into a vessel wall.

A sheath 212 with radiopaque marker 227 is shown in FIG. 10 in its position where it has been pulled back to allow full expansion of the injector tubes 215. There are 3 injector tubes 215 in this embodiment of the INAS. The distal section 220 of the INAS 200 includes the fixed distal wire 225, tapered flexible tip 226, radiopaque marker 224 and sheath engagement section 222 that assures that the distal portion will properly pull back into the sheath 212 following use of the INAS 200 to ablate tissue in a vessel of the human body. Also shown in FIG. 10 are the outer tube 216 with injection lumen 221 and core wire 211. The INAS 200 of FIG. 10 would be used in the same way as the INAS 10 of FIGS. 1 through 5E with the difference being the use of the kinks (double bends) 214 as the penetration limiting members. The kinks 214 being integrated into the injector tubes 215 as compared with the penetration limiter of FIGS. 1-5E which are attached to the injector tubes. Adding the kinks 214 should be a matter of setting a double bend into the shape of the memory metal (e.g. NITINOL) tubing used to form each of the injector tubes 215 that have sharpened ends that form the injection needles 219. In this embodiment the injector tubes themselves limit the penetration into the wall of a target vessel. Processes for shaping and heat treating NITINOL tubing to set the memory are well known.

The present invention has discussed use of the INAS for ablating tissue in the human body. It may also have merit for intravascular injection of any fluid or medication. The ability to limit the depth of penetration allows it to inject any fluid selectively into the media, adventitia or outside of the adventitia of a blood vessel. It is also envisioned that the use of the double bend penetration limiting member concept of FIG. 10 could be applied to any application where fluid injection is required at a preset distance into human tissue.

The term circumferential delivery is defined here as at least three points of simultaneous injection spaced circumferentially within a vessel wall, or circumferential filling of the space outside of the adventitial layer (outer wall) of a blood vessel.

FIG. 11 is a longitudinal cross section of the another embodiment of the present invention INAS 300 in its closed position having four injector tubes 316 that can slide within four guide tubes 315 having expandable distal portions. The injector tubes 316 with sharpened needles 319 have injection egress ports 317 near the distal end of each injector tube 316. A sheath 312 with distal radiopaque marker band 327 encloses the guide tubes 315 with coaxial injector tubes 316. The injector tubes 316 have injection lumens 321. The distal

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end of each of the guide tubes 329 are tapered to provide a surface that will be approximately parallel to the vessel wall when the guide tubes 315 expand outward during deployment. The distal portion of the guide tubes 315 having a length L5 are set in an expanded memory shape and as shown in FIG. 11 are constrained by the sheath 312 to prevent expansion. The four guide tubes 315 are not attached or connected to the core wire 311 over the distance L5. Proximal to the distance L5 the guide tubes 315 are attached or connected to the core wire 311 with the preferred embodiment shown in FIG. 13 where the core wire 311 and four guide tubes 315 are embedded in a plastic cylinder 305.

The INAS 300 distal end has a tapered section 326 attached to a distal shapeable fixed guide wire 320 with wire wrap exterior 325, core wire 311 and tip 328. The tapered section 326 includes a radiopaque marker 324 and proximal taper 323 to facilitate closing the sheath 312 over the proximal section 323 following deployment of the INAS 300 to inject ablative fluid into a vessel wall.

FIG. 12 is an enlargement of the area S12 of the INAS 300 of FIG. 11 showing guide tubes 315 located coaxially inside of the sheath 312. The distal portion of the injector tubes 316 having sharpened needles 319, lumens 321 and injection egress ports 327 are located coaxially inside of the distal portion of the guide tubes 315 with tapered distal ends 329. All or a portion of the needles 319 or the entire injector tube(s) may be made of a radiopaque material such as tantalum, platinum or gold. It is also envisioned that the ends of the needles may be coated or plated with a radiopaque material such as gold or that a platinum insert is placed into the distal tip of the injection tube prior to sharpening the tip into a cutting needle. Also shown are the core wire 311 and the proximal section 323 of the tapered section 326. It is also envisioned that a distal portion including the distal end 329 of the guide tubes 315 may also be made of, coated or plated with a radiopaque material such as gold.

FIG. 13 is a circumferential cross section at S13-S13 of the INAS 300 of FIG. 11 clearly showing the four guide tubes 315 attached to the outside of the core wire 311. The injector tubes 316 with injection lumens 321 are located coaxially inside of the guide tubes 315. The injection tubes 316 are free to slide in the longitudinal direction within the lumens of the guide tubes 315. The injection tubes 316 could also be formed from nitinol and pre-shaped to parallel the curved distal shape of the guide tubes 315 to enhance the coaxial movement of the injector tubes 316 within the guide tubes 315. The guide tubes 315, injection tubes 316 and core wire 311 lie coaxially within the sheath 312 which is free to slide over these parts. It is also shown how the guide tubes 315 and core wire 311 are be embedded in plastic 305 to better hold the parts together or they could be joined by welding, brazing or use of an adhesive. The use of the plastic 305 also allows a cylindrical surface to which the proximal portion of the sheath 312 can seal to allow flushing of the space between the inside of the sheath 312 and the outside of the plastic 305 with saline before the start of device use.

FIG. 14 is a longitudinal cross section of the expanded distal portion of the INAS 300' in the fully open configuration with the injection tubes 316 shown advanced beyond the distal end of the guide tubes 315. The distal end of the injector tubes 316 has the sharpened needles 319 with injection egress ports 317.

In this configuration the sheath 312 has been pulled back to allow the guide tubes 315 to expand outward. The guide tubes 315 are typically made from a memory metal such as NITINOL. The injector tube 316 may be made from any metal, such as 316 surgical grade stainless steel, NITINOL or a

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radiopaque metal such as tantalum or platinum. If the elements 315 and 316 are not fabricated from a radio-opaque metal it is envisioned that distal portion of the injector tube(s) 316 and guide tube(s) 315 would be coated with a radio-opaque material such as gold, typically at or near the distal end of the tube(s) or a piece of radiopaque material may be used to form or be located near the sharpened needles 319 at the distal end of the injector tubes. The diameter L6 denotes the memory configuration for the fully open guide tubes 315. For use in the renal arteries, L6 would typically be between 3 and 10 mm with 8 mm being a best configuration if only one size is made as very few renal arteries are larger than 7 mm diameter. Also shown in FIG. 14 are the distal ends 329 of the guide tubes 315 that in the fully open configuration are approximately parallel to the longitudinal axis of the INAS 300'. The distal portion of the INAS 300' has the tapered section 326 attached to the fixed guide wire 320 with tip 328, outer layer 325 and core wire 311.

FIG. 15 is an enlargement of the area S15 of FIG. 14 as it would appear with the distal end of the injector tube 316 with lumen 321 and distal needle 319 fully advanced beyond the distal end 329 of the guide tube 315. Also shown in FIG. 15 is the arterial wall with internal elastic lamina (IEL), Media, External Elastic Lamina (EEL) and adventitia. FIG. 14 shows that the injection egress ports 317 are placed into the heart of the adventitia.

An important feature of the present invention INAS 300 is that the penetration depth for injection through the injection egress ports is adjustable so that any of the following can be accomplished.

1. Injection into the media
2. Injection into the media and adventitia by positioning one of the injection egress holes in each.
3. Injection into the adventitia as shown in FIG. 15,
4. Injection into both the adventitia and the volume outside of the adventitia and
5. Injection only into the volume outside the adventitia.

Specifically, the distance L7 that the tip of the needle 319 extends beyond the end 329 of the guide tube 315 can be adjusted using the apparatus in the proximal end of the INAS 300

FIG. 16 is a longitudinal cross section of the proximal end of the INAS 300 of FIGS. 11-15. Three handles, the proximal injection handle 330, the central guide tube handle 340 and the distal sheath control handle 350 allow the relative longitudinal movement of the sheath 312, guide tubes 315 and injector tubes 316. The position shown for FIG. 16 has the sheath control handle 350 in its most proximal position which would indicate the sheath 312 has been fully pulled back in the proximal direction which would allow the guide tubes 315 to expand outward as shown in FIG. 14. The gap with distance L8 between the injection handle 330 and the guide tube handle 340 can be adjusted using the screw adjustment piece 334 with screw threads 335 that allow it to move with respect to the proximal portion 333 of the injection handle 330. The gap L8 as set will limit the penetration of the needles 319 and injection egress ports 317 of the injector tubes 316 into the wall of the target vessel. Ideally, a scale can be marked on the proximal portion 333 of the proximal injection handle 330 so that the medical practitioner can set the gap L8 and thus adjust the penetration distance. A luer fitting 338 with access tube 336 is the port for ablative fluid injection into the handle central lumen 332 which is in fluid communication with the lumens 321 of the injector tubes 316.

The central guide tube handle 340 includes an outer portion 342, a sealing member 344 that seals the distal portion of the core wire 311 to the outer portion 342 and provides four holes

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through which the four injector tubes 316 can slide into the proximal ends of the guide tubes 315. A Luer fitting 348 with access tube 346 provides access to the space between the injector tubes 316 and the guide tubes 315 through holes in the guide tubes 347.

The distal sheath control handle 350 includes a distal portion 354 attached to the outside of the sheath 312 with Luer fitting 358 and side tube 356 providing access to the lumen under the sheath 312 to allow it to be flushed with saline before the procedure begins. The handle 350 also has proximal portion 352 and elastic washer 359 that is compressed by screwing the proximal portion 352 into the distal portion 354 to lock the position of the sheath 312 with respect to the guide tubes 315.

FIG. 17 is an enlargement of the area S17 of FIG. 16 showing the injection handle 330 with proximal Luer fitting 338 attached to the side tube 336 with lumen 331. The proximal portion 333 is sealed against the outside of the side tube 336 and also seals against the outside of the four injector tubes 316. This sealing can be by an adhesive or by molding or forming the proximal piece onto the tubes 336 and 316. The lumen 331 of the side tube 336 is in fluid communication with the central lumen 332 of the proximal portion 333 which is in fluid communication with the lumens 321 of the injector tubes 316. Thus an ablative fluid injected through the Luer 338 will flow into the lumens 321 of the injector tubes 316 and will emerge through the injection egress ports 317 shown in FIG. 15 into the tissue in or near the wall of the target vessel. The screw threads 335 on both the proximal portion 333 and screw adjustment piece 334 of the injection handle 330 allow adjustment of the gap L8 of FIG. 16. The gap L8 as set will limit the penetration of the needles 319 and injection egress ports 317 of the injector tubes 316 into the wall of the target vessel. Ideally, a scale can be marked on the proximal portion 333 of the injection handle 330 so that the medical practitioner can set the gap L8 and thus adjust the penetration distance.

FIG. 18 is an enlargement of the area S18 of FIG. 16 showing the central guide tube handle 340 and the sheath control handle 350.

The central guide tube handle 340 includes an outer portion 342, a sealing member 344 that attaches the distal portion of the guide tubes 315 and core wire 311 to the outer portion 342. The outer portion 342 seals against the plastic 305 in which the guide tubes 315 and core wire 311 are embedded. Proximal to the proximal end of the plastic 305, a Luer fitting 348 (shown in FIG. 15) with access tube 346 provides access to the space between the injector tubes 316 and the guide tubes 315 through holes 347 in the guide tubes 315.

The distal sheath control handle 350 includes a distal portion 354 attached to the outside of the sheath 312 with Luer fitting 358 (shown in FIG. 15) and side tube 356 providing access to the lumen between the sheath 312 and the plastic 305 to allow it to be flushed with saline before the procedure begins. The handle 350 also has proximal portion 352 and elastic washer 359 that is compressed by screwing the proximal portion 352 into the distal portion 354 to lock the position of the sheath 312 onto the plastic 305. In this locked position with the INAS 300 closed as shown in FIG. 11 the INAS 300 is advanced into the body until the distal end with the marker band 324 of FIG. 11 is in the renal artery. The proximal portion 352 is then loosened so that the sheath control handle 350 can be pulled in the distal direction while holding the central guide tube handle 340 fixed. It is envisioned that when the proximal end of the sheath control handle proximal piece 352 touches the distal end of the outer portion 342 of the guide tube handle 340 as shown in FIG. 18, that the sheath 312 will

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be full retracted to allow expansion of the guide tubes **315** against the wall of the target vessel.

The full procedure for renal denervation using the INAS **300** is as follows:

1. Remove the sterilized INAS **300** from its packaging in a sterile field, flush the injection lumens **321** of the injector tubes and the space between the sheath **312** and plastic **305** and injector tubes **316** and guide tubes **315** with saline.
2. Access the aorta via a femoral artery, typically with the insertion of an introducer sheath.
3. Using a guiding catheter **80** of FIGS. **5A** through **5E** or a guiding sheath with a shaped distal end, engage the first targeted renal artery through the aorta. This can be confirmed with contrast injections as needed.
4. Place the distal end of the INAS **300** in its closed position of FIG. **11** into the proximal end of the guiding catheter. There is typically a Tuohy-Borst fitting attached to the distal end of a guiding catheter **80** to constrain blood loss.
5. The closed INAS **300** is then pushed through the opened Tuohy-Borst fitting into the guiding catheter.
6. Advance the INAS **300** through the guiding catheter, until the marker band **324** is distal to the distal end of the guiding catheter within the renal artery.
7. Pull the sheath **312** back in the proximal direction while holding the guide tube handle **340** fixed. This will allow expansion of the injector tubes **315** against the wall of the renal artery as shown in FIG. **15**.
8. Lock the sheath control handle **350** down on the plastic **305**.
9. Lock the Tuohy-Borst fitting at the proximal end of the guiding catheter down onto the sheath **312**.
10. Advance the guide tube handle **340** to be sure the distal ends **329** of the guide tubes **315** are in good contact with the wall of the renal artery and flaring outward in order to point more closely to perpendicular to the long axis of the renal artery wall.
11. While holding the guide tube handle **340** fixed, advance the injection handle **330** until its distal end touches the proximal end of the guide tube control handle **340**. This will cause the needles **319** to advance through the distal ends **329** of the guide tubes **315** into the wall of the target vessel to the appropriate penetration limited by the two handles **330** and **340** touching.
12. Attach a syringe or injection system to the Luer fitting **338** that provides ablative fluid that will be injected into the wall of the renal artery. One could optionally inject an anesthetic drug like lidocaine and/or contrast media before the ablative fluid to prevent or reduce the pain associated with the procedure and/or ensure the needles are in the right position. It is also conceived that an anesthetic or contrast can be combined with the ablative fluid.
13. Inject an appropriate volume of the ablative fluid from the syringe or injection system through the lumens **321** of the injector tubes and out of the injection egress ports **317** into and/or outside of the wall of the renal artery. A typical injection would be 1-10 ml. This should produce a multiplicity of intersecting volumes of ablation (one for each needle) that should create a torroid of ablated tissue around the circumference of the renal artery as shown as the ablated regions shown in FIGS. **5D** and **5E**.
14. While holding the guide tube handle **340** fixed. Pull the injection handle **330** in the proximal direction retracting the needles **319** back into the guide tubes **315**.

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15. Unlock the sheath control handle **350** from the plastic **305** and while holding the guide tube control handle **340** fixed, advance the sheath control handle **350** in the distal direction until the guide tubes **315** are fully collapsed back into the distal end of the sheath **312** and the marker bands **327** and **324** are next to one another indicating that the INAS **300** is now in its closed position as shown in FIG. **11**.

16. The same methods as per steps 6-15 can be repeated to ablate tissue around the other renal artery during the same procedure.

17. Remove the INAS **300** in its closed position from the guiding catheter. Being in the closed position, the needles **319** are doubly enclosed within the guide tubes **315** which are inside the sheath **312** so the sharpened needles **319** cannot harm the health care workers, or expose them to blood borne pathogens.

18. Remove all remaining apparatus from the body.

A similar approach can be used with the INAS **300**, to treat atrial fibrillation through a guiding catheter inserted through the septum into the left atrium with the wall of the target vessel being the wall of one of the pulmonary veins.

FIG. **19** is a longitudinal cross section of the proximal portion of an alternate embodiment of the INAS **400** which simplifies the design as compared to the INAS **300** proximal portion of FIG. **16**. The INAS **400** uses the identical distal portion design as the INAS **300** of FIGS. **11-15**. Three handles, the proximal injection handle **430**, the central guide tube handle **440** and the distal sheath control handle **450** allow the relative longitudinal movement of the sheath **312**, middle tube **415** and inner tube **416** with injection lumen **421**. The position shown for FIG. **19** has the sheath control handle **450** near its most proximal position which would indicate the sheath **312** has been pulled back in the proximal direction. In this position, as with the INAS **300** of FIGS. **11-18** this will cause the distal portion of the guide tubes **315** to expand outward as shown in FIG. **14**.

The gap with distance **L9** between the injection handle **430** and the guide tube handle **440** can be adjusted using the screw adjustment piece **434** with screw threads **435** that allow it to move with respect to the proximal portion **433** of the proximal injection handle **430**. The proximal end of the screw adjustment piece **434** is the penetration limiting member that will limit to the distance **L9**, the penetration of the needles **319** and injection egress ports **317** of the injector tubes **316** into the wall of the target vessel. Ideally, a scale can be marked on the proximal portion **433** of the injection handle **430** so that the medical practitioner can set the gap **L9** and thus adjust the penetration distance. The central tube **416** with lumen **421** is sealed into the proximal piece **433** of the proximal injection handle **430**. A luer fitting **438** with access tube **436** is the port for ablative fluid injection into the handle lumen **432**. The lumen **439** of the Luer fitting **438** is in fluid communication with the lumen **437** of the access tube **436** which is in fluid communication with the injection lumen **421** of the inner tube **416**. The inner tube **416** is typically a metal hypertube although a plastic tube or plastic tube with braided or helical wire reinforcement is also conceived.

The central guide tube handle **440** attached to and controlling the longitudinal movement of the middle tube **415** includes a proximal portion **444** that can screw into a distal portion **442**. When screwed in to the distal portion **442**, the proximal portion **444** will compress the washer **445** allowing the handle **440** to be locked down onto the middle tube **415**. This is also needed during preparation for use when the Luer

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fitting 448 with side tube 446 can be used to flush the space between the inner tube 416 and middle tube 415 with saline solution.

The distal sheath control handle 450 attached to and controlling the longitudinal movement of the sheath 312 includes a proximal portion 454 that can screw into a distal portion 452. When screwed in to the distal portion 452, the proximal portion 454 will compress the washer 455 allowing the handle 450 to be locked down onto the sheath 312. This is also needed during preparation for use when the Luer fitting 458 with side tube 456 can be used to flush the space between the middle tube 415 and sheath 312 with saline solution.

A removable spacer 449 that prevents advancement of the injection handle 430 will help ensure that the needles are not accidentally advanced before the INAS 400 is on its open position inside the renal artery. It is also conceived that the handles can be color coded or numbered to facilitate the proper order of use. For example the sheath control handle labeled "1" is pulled back first the spacer 449 labeled "2" is removed and then the injection handle 430 labeled "3" can be advanced.

FIG. 20 is a longitudinal cross section of a central transition portion 460 connecting the proximal portion of the INAS 400 of FIG. 19 with the distal portion of the INAS 300 of FIGS. 11-15. The proximal end of the central transition portion 460 includes the same three concentric tubes located at the distal end of the handle portion of the INAS 400 shown in FIG. 19. Specifically, the proximal end of the transition portion 460 includes the inner tube 416 with injection lumen 421, the middle tube 415 and the sheath 312. At the distal end of the inner tube 416, a manifold 410 is inserted which seals the inner tube 416 to the four injector tubes 316 such that the lumen 421 of the inner tube 416 is in fluid communication with the lumens 321 of the four injector tubes 316. In addition, longitudinal motion of the inner tube 416 will therefore be translated to longitudinal motion of the four injector tubes 316.

The middle tube 415 seals inside of the plastic member 405 which also seals to the guide tubes 315 and core wire 311. Longitudinal motion of the middle tube 415 will translate into longitudinal motion of the four guide tubes 315. The sheath 312 is the same sheath as in the distal portions of the INAS 300 of FIGS. 11-15.

FIG. 21 is a circumferential cross section at S21-S21 of the central transition section 460 of FIG. 20. Looking in the distal direction, one sees in cross section, the three concentric tubes the sheath 312, middle tube 415 and inner tube 416. Inside the inner tube one sees the proximal end of the manifold 410 and the proximal ends of the four injector tubes 316. It can clearly be seen that the manifold 410 seals the four injector tubes 316 into the inner tube 416 and the lumens 321 of the injector tubes 316 open into the lumen 421 of the inner tube 416.

FIG. 22 is a circumferential cross section at S22-S22 of the central transition section 460 of FIG. 20. Looking in the distal direction one sees in cross section, the sheath 312 and middle tube 415. The middle tube 415 is sealed into the distal portion of the plastic member 405. One also sees the proximal end of the four guide tubes 315 and core wire 411. It also shows how the four injector tubes 316 enter the proximal ends of the guide tubes 315.

FIG. 23 is a circumferential cross section at S23-S23 of the central transition section 460 of FIG. 20. This cross section is identical to the circumferential cross section shown in FIG. 13 showing the sheath 312 and plastic member 405 (was 305 in FIG. 13) that seals and attaches together the four guide tubes 315 and the core wire 311. The injector tubes 316 lie concentrically inside of the four guide tubes 315. Thus, FIGS.

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20-23 clearly show how the simplified proximal end of FIG. 19 connects to the distal portion of the INAS 300 of FIGS. 11-15.

FIG. 24 is a schematic view of yet another embodiment of the distal portion of the present invention Intravascular Nerve Ablation System (INAS) 500 in the fully open configuration with the injection tubes 516A, 516B, 516C and 516D (516A-D) shown advanced beyond the distal end of the guide tubes 515A, 515B, 515C and 515D (515A-D) respectively. The distal end of the injector tubes 516A-D have the sharpened needles 519A-D with injection egress ports 517.

In this configuration the sheath 512 has been pulled back to allow the guide tubes 515A-D to expand outward. The guide tubes 515A-D are typically made from a memory metal such as NITINOL. The injector tube 516A-D may be made from any metal such as titanium, stainless steel, NITINOL or a radiopaque metal such as tantalum or platinum. If the elements 515A-D and/or 516A-D are not fabricated from a radiopaque metal it is envisioned that distal portion of the injector tubes 516A-D and guide tubes 515A-D could be coated with a radiopaque material such as gold, typically at or near the distal end of the tube(s) or a piece of radiopaque material may be used to form or be located near the sharpened needles 519A-D at the distal end of the injector tubes. The diameter L10 denotes the memory configuration for the fully open guide tubes 515. For use in the renal arteries, L10 would typically be between 5 and 10 mm with 8 mm being a best configuration if only one size is made as very few renal arteries are larger than 7 mm diameter. Also shown in FIG. 24 are the distal ends 529A-D of the guide tubes 515A-D that in the fully open configuration are approximately parallel to the longitudinal axis of the INAS 500'. The distal portion of the INAS 500 has the tapered section 526 attached to the fixed guide wire 520 with tip 528, outer layer 525 and core wire 511. The significant difference between the INAS 500 of FIG. 24 and the INAS 300' of FIG. 14 is the longitudinal offset between the distal ends 529 A-D of the guide tubes 515A-D which will cause the injection egress points associated with each of the injector tubes 516A-D to be offset in the longitudinal direction. The longitudinal offset distance L11 is shown between adjacent injector tubes 516A and 516B and between 516B and 516C. The longitudinal offset difference L11 can be as small as 1 mm and as long as 25 mm although the most desirable offset would be between 5 mm and 10 mm is envisioned. The advantage of the longitudinal offset that creates a helical ablation pattern is to reduce circumferential injury to the artery to prevent vessel failure or late vascular contraction that is seen in balloon angioplasty from scar tissue formed in the arterial tissue. The offset ablation of the INAS 500 will still substantially ablate the sympathetic nerves with less potential risk of late complications from negative arterial remodeling. The helical pattern of ablation has been shown to work in studies of RF ablation and should therefore also work with injection of an ablative solution.

While the INAS 500 shows four injector tubes 516A-D, it is envisioned that as few as two and as many as eight injector tubes with injection egress can be used. The preferred embodiment for renal denervation is three or four.

While this description has focused on use of the INAS for use in ablation of tissue, it is also clearly envisioned that the apparatus and methods of FIGS. 1-23 can be applied to the use of this apparatus to inject any fluid for any purpose including that of local drug delivery into a specified portion of a blood vessel or the volume of tissue just outside of a blood vessel.

Various other modifications, adaptations, and alternative designs are of course possible in light of the above teachings.

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Therefore, it should be understood at this time that within the scope of the appended claims the invention may be practiced otherwise than as specifically described herein.

What is claimed is:

1. An intravascular nerve ablation system for circumferential delivery of an ablative fluid to a volume of tissue in proximity to a vessel wall of a target vessel comprising:

a catheter body having a central axis extending in a longitudinal direction and a fluid injection lumen;

at least a first and second guide tube, each guide tube having a distal end and a central lumen, each guide tube having a distal portion that is expandable between a first position aligned with the axis and a second position inclined away from the axis;

at least a first and second injector tube, each injector tube having an injection lumen for delivering the ablative fluid, the first and second injector tubes located coaxially inside of the first and second guide tubes respectively, each injector tube having a sharpened injection needle at its distal end, each injection needle having injection egress near its distal end, the first and second injector tubes being adapted to simultaneously slide within the first and second guide tubes respectively; and

a penetration depth limitation mechanism comprising an injector tube handle and a guide tube handle configured to allow the relative longitudinal movement of the guide tubes and the injector tubes, wherein a gap between the injector tube handle and the guide tube handle is configured for simultaneously limiting the depth of penetration of the injection needles into the vessel wall of the target vessel.

2. The system of claim 1 further including a sheath, the sheath located coaxially outside of the catheter body, the sheath having a closed position and an open position, the open position allowing the first and second guide tubes to expand outward against the inside of the wall of the target vessel.

3. The system of claim 2 further including a sheath control handle and labeling, the sheath control handle being attached to the proximal end of the sheath, the sheath control handle adapted to control the longitudinal motion of the sheath, the labeling selected from at least one of the types from the group consisting of roman alphanumeric letters, numbers, words, arrows, and directional indicators.

4. The system of claim 1 where the circumferential delivery of the ablative fluid is in a circular pattern.

5. The system of claim 1 where the circumferential delivery of the ablative fluid is in a helical pattern.

6. The system of claim 1 wherein the injector tube handle located near the proximal end of the catheter body includes a port for receiving the ablative fluid, the injector tube handle further adapted to control the distal and proximal movement of the injector tubes.

7. The system of claim 1, wherein the injection needles are less than 25 gauge.

8. The system of claim 2, comprising a radiopaque marker on the sheath.

9. The system of claim 1, comprising a radiopaque marker on the first guide tube.

10. The system of claim 1, including between 4 and 12 guide tubes.

11. The system of claim 1, wherein the first and second guide tubes are equally spaced around a circumference of the catheter body.

12. The system of claim 1 further comprising a guide tube control mechanism connected to the first and second guide

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tubes, the guide tube control mechanism adapted to control the simultaneously longitudinal movement of the first and second guide tubes.

13. The system of claim 12 further comprising an injector tube control mechanism connected to the first and second injector tubes, the injector control mechanism adapted to control the longitudinal movement of the first and second injector tubes.

14. The system of claim 1 further comprising an injector tube control mechanism connected to the first and second injector tubes, the injector control mechanism adapted to control the longitudinal movement of the first and second injector tubes.

15. An intravascular nerve ablation system for circumferential delivery of an ablative fluid to a volume of tissue in proximity to a vessel wall of a target vessel comprising:

a catheter body having a central axis extending in a longitudinal direction and a fluid injection lumen;

a first guide tube having a distal end and a central lumen, the first guide tube having a distal portion adapted to expand outward;

a first injector tube having an injection lumen in fluid communication with the fluid injection lumen of the catheter body, a portion of the first injector tube located coaxially inside of the first guide tube, the first injector tube having a first sharpened injection needle at its distal end, the first injection needle having a first injection egress near its distal end, the first injector tube being adapted to slide in the distal and proximal directions within the first guide tube;

a second guide tube having a distal end and a central lumen, the second guide tube having a distal portion adapted to expand outward;

a second injector tube having an injection lumen in fluid communication with the fluid injection lumen of the catheter body, a portion of the second injector tube located coaxially inside of the second guide tube, the second injector tube having a second sharpened injection needle at its distal end, the second injection needle having a second injection egress near its distal end, the second injector tube being adapted to slide in the distal and proximal directions within the second guide tube;

an injector tube control mechanism connected to the first injector tube and the second injector tube, the injector control mechanism adapted to control the longitudinal movement of the first injector tube and the second injector tube; and

a penetration depth limitation mechanism comprising an injector tube handle and a guide tube handle configured to allow the relative longitudinal movement of the guide tubes and the injector tubes, wherein a gap between the injector tube handle and the guide tube handle is configured for simultaneously limiting the depth of penetration of the first injection needle and the second injection needle into the vessel wall of the target vessel.

16. The system of claim 15 further including a sheath having a sheath control mechanism at its proximal end, the sheath located coaxially outside of the catheter body, the sheath having a closed position and an open position, the open position allowing the first guide tube and the first injector tube to expand outward to facilitate delivery of an ablative fluid to the wall of the target vessel.

17. The system of claim 16 further including labeling to indicate the order of use of at least one of the sheath control mechanism and the injector tube control mechanism, the labeling chosen from at least one of the types selected from

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the group consisting of roman alphanumeric letters, numbers, words, arrows, and directional indicators.

18. The system of claim 16 further including a tapered distal portion that in combination with the sheath completely enclose the first injection needle and the second injection needle when the sheath is in its closed position.

19. The system of claim 16 further including a radiopaque marker in proximity to the distal end of the sheath.

20. The system of claim 15 where the circumferential delivery of the ablative fluid is in a helical pattern.

21. The system of claim 15 further including a component to prevent advancement of the injector tube control mechanism in the distal direction.

22. The system of claim 15 where the circumferential delivery of the ablative fluid is into a specific volume of tissue selected from at least one of the group consisting of: the media of the wall of the target vessel, the adventitia of the wall of the target vessel, the volume outside of the adventitia of the wall of the target vessel, the media and adventitia of the wall of the target vessel, and the adventitia and the volume outside of the adventitia of the target vessel.

23. The system of claim 15 where the circumferential delivery includes at least three points of injection egress.

24. The system of claim 15 where said catheter body includes a fixed guide wire attached to its distal end.

25. The system of claim 15 configured to have a portion of the system advanced coaxially over a separate guide wire.

26. The system of claim 15 where the distal portion of the first guide tube is self-expanding.

27. The system of claim 26 further including a sheath that when retracted to its most proximal open position allows the first guide tube self-expanding portion to expand outward.

28. The system of claim 15 where the distal portion of the first injector tube is self-expanding.

29. The system of claim 28 where the self-expanding portion is formed from NITINOL.

30. The system of claim 15 where said ablative fluid includes at least one of the ablative fluids selected from the group consisting of: ethanol, phenol, glycerol, lidocaine, bupivacaine, tetracaine, benzocaine, guanethidine, and botulinum toxin.

31. The system of claim 15 where said ablative fluid is a heated fluid composition.

32. The of claim 15 where said ablative fluid is a cooled fluid composition.

33. The system of claim 15 where said ablative fluid is a form of steam injected through the injection lumen of the catheter body.

34. The system of claim 15, wherein the injector tube control mechanism and the penetration depth limitation mechanism are located on a proximal portion of the system.

35. The system of claim 15, wherein the injector tube control mechanism and the penetration depth limitation mechanism are located on a proximal handle.

36. An intravascular nerve ablation system for circumferential delivery of an ablative fluid to a volume of tissue in proximity to a vessel wall of a target vessel comprising:

a catheter body having a central axis extending in a longitudinal direction and a fluid injection lumen;

a first guide tube having a distal end and a central lumen, the first guide tube having a distal portion adapted to expand outward;

a first injector tube having an injection lumen in fluid communication with the fluid injection lumen of the catheter body, a portion of the first injector tube located coaxially inside of the first guide tube, the first injector tube having a first sharpened injection needle at its distal

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end, the first injection needle having a first injection egress near its distal end, the first injector tube being adapted to slide in the distal and proximal directions within the first guide tube;

a second guide tube having a distal end and a central lumen, the second guide tube having a distal portion adapted to expand outward;

a second injector tube having an injection lumen in fluid communication with the fluid injection lumen of the catheter body, a portion of the second injector tube located coaxially inside of the second guide tube, the second injector tube having a second sharpened injection needle at its distal end, the second injection needle having a second injection egress near its distal end, the second injector tube being adapted to slide in the distal and proximal directions within the second guide tube;

a guide tube control mechanism connected to the first guide tube and the second guide tube, the guide tube control mechanism adapted to control the simultaneously longitudinal movement of the first guide tube and the second guide tube; and

a penetration depth limitation mechanism comprising an injector tube handle and a guide tube handle configured to allow the relative longitudinal movement of the guide tubes and the injector tubes, wherein a gap between the injector tube handle and the guide tube handle is configured for simultaneously limiting the depth of penetration of the first injection needle and the second injection needle into the vessel wall of the target vessel.

37. The system of claim 36 further including a sheath having a sheath control mechanism at its proximal end, the sheath located coaxially outside of the catheter body, the sheath having a closed position and an open position, the open position allowing the first guide tube and the first injector tube to expand outward to facilitate delivery of an ablative fluid to the wall of the target vessel.

38. The system of claim 37 further including a tapered distal portion that in combination with the sheath completely enclose the first injection needle and the second injection needle when the sheath is in its closed position.

39. The system of claim 37 further including a radiopaque marker in proximity to the distal end of the sheath.

40. The system of claim 36 where the circumferential delivery of the ablative fluid is in a helical pattern.

41. The system of claim 36 where the circumferential delivery of the ablative fluid is in a circular pattern.

42. The system of claim 36 where the circumferential delivery of the ablative fluid is into a specific volume of tissue selected from at least one of the group consisting of: the media of the wall of the target vessel, the adventitia of the wall of the target vessel, the volume outside of the adventitia of the wall of the target vessel, the media and adventitia of the wall of the target vessel, and the adventitia and the volume outside of the adventitia of the target vessel.

43. The system of claim 36 where the circumferential delivery includes at least three points of injection egress.

44. The system of claim 36 where said catheter body includes a fixed guide wire attached to its distal end.

45. The system of claim 36 configured to have a portion of the system advanced coaxially over a separate guide wire.

46. The system of claim 36 where the distal portion of the first guide tube is self-expanding.

47. The system of claim 46 further including a sheath that when retracted to its most proximal open position allows the first guide tube distal self-expanding portion to expand outward.

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48. The system of claim **36** where the distal portion of the first injector tube is self-expanding.

49. The system of claim **48** where the self-expanding portion is formed from NITINOL.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 9,056,185 B2
APPLICATION NO. : 13/342521
DATED : June 16, 2015
INVENTOR(S) : Fischell et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Specification

In column 13 at line 67, Change “wire” to --wire 11.--.

In column 26 at line 41, Change “5168” to --516B--.

In column 26 at line 42, Change “5168” to --516B--.

In the Claims

In column 29 at line 44, In Claim 32, change “The of” to --The system of--.

Signed and Sealed this
Third Day of May, 2016



Michelle K. Lee
Director of the United States Patent and Trademark Office